STANFORD UNIVERSITY BIOMEDICAL APPLICATIONS TEAM

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1978

ANNUAL REPORT

NASA Technology Utilization

Grant No. NGR 05-020-634

PREFACE

This report summarizes the Stanford University-NASA Biomedical Applications Team's activities for the period January 1, 1978 through December 31, 1978. This program is under the direction of Donald C. Harrison, M.D., Chief of the Division of Cardiology, Stanford University School of Medicine. The Stanford Biomedical Applications Team is funded by NASA Grant NGR 05-020-634 and its technical monitor is Harold Sandler, M.D., Chief of the Biomedical Research Division, NASA-Ames Research Center.

For the convenience of the reader, the names and addresses of medical device manufacturers referred to in this report are included in Appendix B. This listing does not constitute an endorsement by either the National Aeronautics and Space Administration or the Stanford University School of Medicine.

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ANNUAL REPORT SUMMARY

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This report reviews the major activities of the Stanford University Biomedical Technology Transfer Program which is funded by NASA to apply aerospace science and engineering expertise to the solution of significant biomedical engineering problems. During the preceding year, substantial progress has been made in the identification of appropriate technological problems, incorporation of NASA engineering into the design and fabrication of potential solutions, laboratory and clinical evaluation of new technology, and the adoption of this technology by medical device manufacturers. Progress on the 14 active biomedical technology transfer projects, described in detail in this report, is summarized in the list which follows:

1. Intracranial Pressure Monitoring - The prototype system has been successfully implanted in 7 neurosurgical patients for postoperative monitoring. A contract has been signed for commercial development of a second-generation system and substantial design improvements have been reviewed and accepted.

2. Noninvasive Cardiovascular Measurements Conference - This international symposium was attended by 241 representatives of industry, government, and academia, both in the medical and engineering fields. The sessions highlighted contributions of NASA technology using a variety of noninvasive diagnostic modalities to obtain quantitative information about the heart

and circulatory system. The proceedings of the Conference are being prepared for publication.

3. Liquid Circulating Garments - Temperature regulating carts and garments have been shipped to a number of medical investigators. Although some clinical trials have begun, the numbers of subjects involved at the time of this report is too small to be conclusive.

4. Versatile Portable Speech Prosthesis - All system components have been received and tested. The contribution of an additional speech synthesizer by industry has made it feasible to construct both a developmental system and a clinical system. The project is on schedule for demonstration (involving a cerebral palsy patient) in June, 1979. Two companies have expressed strong interest in incorporating various features of the speech prosthesis into their communications aids for the handicapped.

5. Purkinje Image Eyetracker - Fabrication of a simplified, self-aligning, clinical monocular eyetracker is nearly complete. Preliminary results of a pilot study involving the early detection of neurological disorders are reported.

6. Nanophor - This clinical laboratory instrument has now been licensed to a manufacturer. The BATeam has assisted in the preparation of an instruction manual and identified laboratories at Stanford University Medical School willing to conduct an evaluation of this new instrument.

7. Spatial Frequency Multiplexing - The research laboratory has been moved from the Engineering Bldg. to the Stanford University Medical School to facilitate collaboration with the Departments

of Radiology and Cardiology in patient studies. One of the leading manufacturers of advanced x-ray equipment has made a definite committment to assist in R&D leading to commercialization.

9. Pediatric Roentgen Densitometry - An improved x-ray detection array has been specified and three systems are being assembled for expanded clinical trials in leading university cardiology departments.

10. Wristcom - The operational breadboard has been demonstrated to both the National Center for the Deaf-blind and the Smith-Kettlewell Institute. This communications device was also demonstrated at the Interagency Conference on Rehabilitative Engineering. Packaging of the integrated hybrid circuitry is underway.

11. EMG Biotelemetry for Pediatrics - This NASA-designed system has been coupled to a minicomputer for automated analysis of gait abnormalities and is in routine use at the Children's Hospital at Stanford. The telemetry system is now commercially available and improvements requiring change from discrete component to hybrid circuit design are under consideration.

12. Bone Mechanical Impedance - Tests conducted this year in the Orthopedics Out-patient Department have demonstrated the reproducibulity and feasibility for a noninvasive determination of bone properties. The continued clinical trials, in cooperation with the Lipid Research Center at Stanford, have been agreed upon in order to determine any limitations in measuring small

changes in bone properties over long periods of time.

13. Cardiovascular Magnetic Measurements - Approval of NIH funding for related studies has permitted proceeding with this NASA technology transfer. Preliminary calculations, specifications, and design of a magnetic coil system and associated power supplies and magnetometers has begun.

14. ICU Synthesized Speech Alarm System - This new project has recently received NASA approval and an interagency transfer of funds between NASA and the Veterans Administration is in progress.

In addition to these active technology transfer projects, four new biomedical engineering problems have been received and are in various preliminary stages of specification of technical needs, search for relevant NASA technology, and market analysis.

Overall, this has been an extremely active and productive year, as is evidenced by the number of projects entering into the clinical evaluation and commercialization phases of the technology transfer process. The Biomedical Technology Transfer Program at Stanford is finding new applications for NASA technology as well as successfully transferring these solutions to an increasing number of medical problems.

INTRODUCTION

INTRODUCTION

Background

The Biomedical Technology Transfer Program was established by NASA in 1966 for the specific purpose of transferring aerospace technology to the solution of biomedical problems. Biomedical Applications Teams (BATeams) interface with the medical profession and NASA scientists and engineers in order to facilitate the application of NASA technology to significant medical and biological problems. There are three BATeams, located at the following institutions:

1. Stanford University School of Medicine
   Cardiology Division
   701 Welch Road
   Suite 3301
   Palo Alto, California 94304

2. Research Triangle Institute
   P.O. Box 12194
   Research Triangle Park, North Carolina 27709

3. Advisory Center for Medical Technology and Systems
   University of Wisconsin
   1500 Johnson Drive
   Madison, Wisconsin 53706

The Teams are funded and coordinated by the Technology Utilization Office in Washington, D.C.

Technology Transfer Process

BATeam members meet with medical and biological science investigators in order to define significant problems to which NASA technology may be applied. The term "technology" includes hardware (scientific instruments and test facilities) and software (computer programs and technical reports resulting from aerospace research and development). The most important facet of NASA technology is the expertise of its scientists and engineers. The BATeam depends on them for innovative solutions to challenging biomedical problems.

There are many different ways to apply or transfer technology developed through the Space Program to solving biomedical problems. The following general procedure is followed by the BATeams:

1. A Team representative confers with the medical scientist or clinician who originated the problem. During this meeting a Problem Statement is developed, including:

   A. General medical background.

   B. Specific technical needs.

   C. Engineering constraints and specifications.

   D. Facilities, staff, and funding available to implement the proposed solution.

   E. Previous inadequate solutions.

   F. Suggested references.

2. In order to qualify for BATeam acceptance, the Problem Statement must satisfy the following criteria:

   A. No ready solution is available through commercial medical instrument manufacturers.

   B. The problem can be defined in such terms that aerospace related technology could be applicable to a solution.

   C. Solution of the problem would make a significant contribution to medical research or clinical medical practice.

3. The biomedical problem must then be matched to relevant NASA technology:

   A. A manual or computer search of the aerospace data banks is made by one of NASA's six Industrial Centers. Computer searches may utilize the NASA Scientific and Technical Information Facility at Baltimore/Washington International Airport, Maryland.

B. The Team evaluates available commercial technology to determine what is presently available.

C. The Problem Statement, formulated during the initial interview, is circulated among scientists and engineers who have been selected by the Team, the Technology Utilization Offices, or Headquarters.

D. Team members contact NASA personnel who have done work related to the specific problem requirements. These NASA engineers are frequently contacted through the Field Centers' Technology Utilization Offices.

4. Potential NASA solutions are presented to the problem originator, along with supporting data.

The problem originator and the Team then work together to evaluate the potential solutions. Their decision to implement a proposed solution will depend upon:

A. Assessment of technical feasibility.

B. Medical acceptability.

C. Cost and time necessary for implementation.

D. Assessment of commercial potential.

Adaptive Engineering

If, after careful screening, a problem is found to be medically significant and has a potential NASA technological solution, the Team attempts to effect a transfer. Instrumentation originally designed for the Space Program can seldom be directly applied to a biomedical problem. It must be modified or re-engineered for the new research or clinical application. Usually the problem originator requries engineering assistance to modify and implement the NASA technology. Redesign and adaptive engineering frequently require material and engineering resources of the Team, NASA, and/or a medical device manufacturer.

The resulting prototype device must be clinically tested to demonstrate that it meets specified engineering and medical standards. In order for the new approach to be accepted by the medical community, papers must be presented at major medical and engineering symposia and published in leading medical journals. Even when all of these steps have been taken, the new biomedical device cannot achieve widespread use until it becomes commercially available.

Cost sharing opportunities are explored with NASA, the National Institute of Health, the Rehabilitative Services Administration, and the Veteran's Administration. The required co-funding is solicited from the Government agency which has the primary responsibility for the particular medical area. For example, if the medical problem involved a diagnostic cancer technique, the National Cancer Institute would be asked to provide co-funding. If NASA funding is needed and can be justified, the Team will work closely with the appropriate NASA Field Center's Technology Utilization Office. Together they will prepare the Research and Technology Objectives and Plans (RTOP), a formal research proposal, for submission to NASA Headquarters.

Commercialization

1. Criteria

   A new technology application can reach the commercial market more easily if the following criteria are met:

   A. The NASA technological solution provides an improvement in treatment or diagnosis.

   B. The solution provides a reduction in health care costs.

C. The market is large enough for the necessary capital risk.

D. The instrumentation can be manufactured at a cost which will permit penetration of the market.

E. The identified manufacturer is willing to bear most of the additional development cost.

2. Strategy

Since widespread impact and utilization is the ultimate goal, a survey of the potential market is conducted early in the transfer process. The market survey is conducted with the help of potential manufacturers and the Illinois Institute of Technology - Research Institute (IITRI). Physicians' estimates of the number of patients who would benefit from the new technology also are an important part of this survey.

If the market survey is favorable, suitable manufacturers are contacted by the Team. Manufacturing representatives are interviewed, and working agreements and licensing arrangements are negotiated. The Team reviews product development and marketing plans, and the cost of carrying out these plans is estimated.

Stanford Biomedical Applications Team

The Stanford BATeam is composed of a multidisciplinary group of scientists, physicians, and engineers who work in close cooperation with NASA Field Center personnel and, in particular, with biomedical and engineering groups at NASA-Ames Research Center (ARC), Moffett Field, California. The Stanford BATeam is part of the Stanford University School of Medicine's Cardiology Division and emphasizes applying NASA-developed technology to the solution of urgent problems regarding the diagnosis and treatment of heart disease. Previous applications of aerospace technology to this medical specialty have included projects in electrocardiography, cardiac catheterization, biomedical electrodes, and ultrasonic cardiac imaging. In addition to cardiology, the Stanford BATeam has found new applications for space technology in such diverse medical specialties as: cerebral palsy, neurosurgery, orthopedics, communicative disorders, pediatrics, oncology, and radiology.

The principal members of the Stanford BATeam are:

- Donald C. Harrison, M.D.
  Director
  Chief, Cardiology Division

- Gene Schmidt, M.D.
  Assistant Director

- Luke Brennan, M.E.B.M.E.
  Biomedical Engineer

- Harry Miller
  Deputy Director

- Edwin Alderman, M.D.
  Richard Popp, M.D.

  Assistant Professors of Cardiology

- Marilyn Anderson
  Program Secretary

- Bill Haskell, Ph.D.
  Physiologist

- Droni Moo
  Conference Coordinator

- Steve Corbin, Ph.D
  Bioengineer

- Robert Debs
  Paul Purser
  Robert Zimmerman

  Part-time Engineering Consultants

These Stanford Team members work in close cooperation with personnel at NASA-Ames Research Center. The Ames group includes:

- Harold Sandler, M.D.
  Technical Monitor
  Chief, Biomedical Research Division

- Walter Goldenrath
  Ames-WESRAC Technical Coordinator

- Cleve Foss
  Herb Holley
  Charles Kubokawa

  Technology Utilization Officers

- Thomas Fryer
  Robert Lee

  Electronic Instrument Development Branch

- Salvador Rositano
  Richard Westbrook

  Electronic Systems Engineering Branch

- Thomas Wempe
  Manned Vehicle Systems Research Division

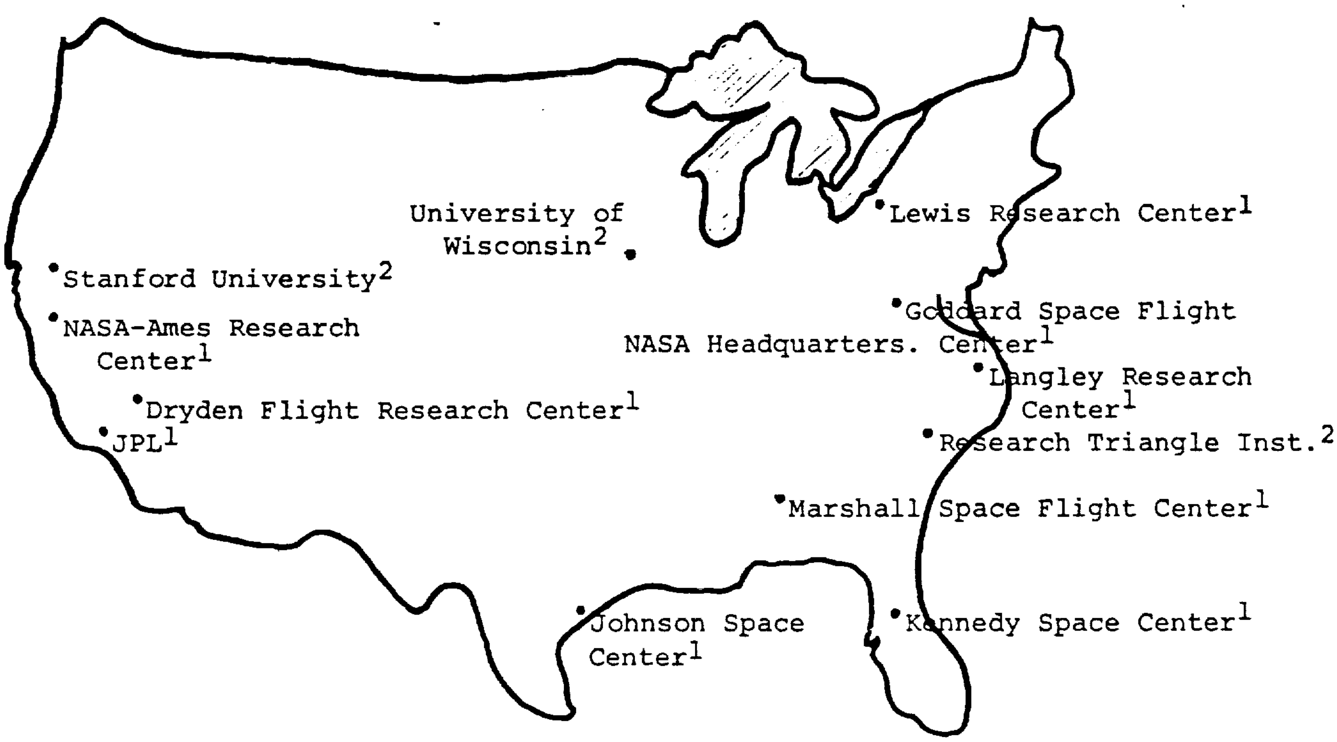
- Bruce Webbon
  Bill Williams

  Advanced Life Support Division

- Ernest Iufer
  Magnetic Standards Laboratory

- Darrell Brekke
  Patent Counsel

Additional help is applying aerospace solutions to important medical problems is obtained from other NASA Field Centers[1] and Biomedical Applications Teams[2], as shown on the following map:



TECHNOLOGY TRANSFER PROJECTS

INTRACRANIAL PRESSURE MONITORING

Objective

Evaluation and commercialization of a NASA-developed intracranial pressure monitoring system.

Background

In cases of head trauma, brain tumor, cerebral infection, and hydrocephalus the pressure inside the head or intracranial pressure (ICP) can become markedly elevated. As ICP increases it can cause reduced blood flow to brain cells resulting in brain damage. If an ICP rises to certain critical levels, it can cause a complete shut-down of blood flow to the brain resulting in irreversible brain damage or death within a few minutes. It is, therefore, vital to the optimal management of he brain-injured patient to have a continuous and accurate technique for monitoring ICP. As ICP begins to rise there are medical and surgical therapies which can be instituted. An osmotic diuretic can be administered to reduce brain swelling and lower blood pressure. Likewise, steroids are believed to have a beneficial effect in cases of increased ICP. Placing the patient on a respirator and lowering blood CO_2 will reduce intracranial pressure, and cause a more optimal redistribution of blood flow. Barbiturates can be given to decrease cerebral oxygen consumption. Finally, such surgical procedures as tying off a bleeding vessel, draining an abscess, or removing a portion of the skull, can be perfomed

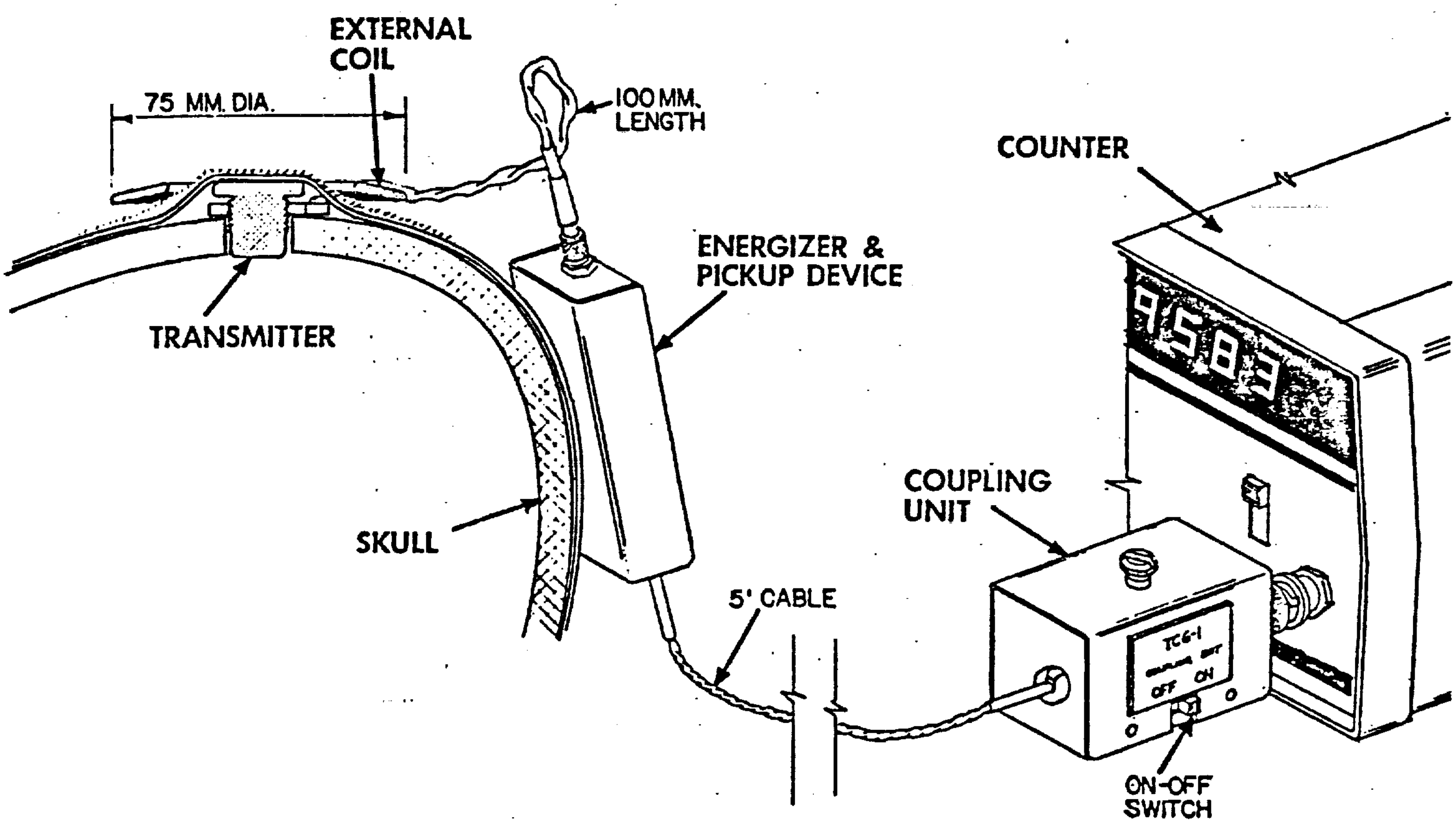


FIGURE 1
ICPM System

depending upon the type of brain injury. However, the decision to implement these therapies and to adequately monitor the patient during the therapy requires a reliable ICP monitoring system.

NASA Technology

An intracranial pressure monitor, consisting of an implanted epidural pressure transducer/transmitter, and an external/receiver, was developed by the NASA-Ames Research Center as a response to a request for assistance by the Department of Neurosurgery at Stanford University Medical School. The system makes extensive use of NASA technology. The pressure transducer, which senses pressure transmitted through the cerebrospinal fluid and dura (a fibrous membrane which surrounds the brain) was originally developed at Ames for the measurement of air pressure over the wings of experimental aircraft during wind tunnel tests. The inductively-powered biotelemetry electronics were likewise developed as a part of the Ames Research Center Life Sciences Program for monitoring man and animals in space.

Approach (See Fig. 1.)

The ICPM transmitter is mounted in a small burr hole which is drilled in the skull by the neurosurgeon. Its active capacitive diaphragm is positioned coplaner with the dura and locked in place. The scalp is then sutured close over the transmitter. The transmitter responds to changes in ICP by transmitting a frequency modulated signal to an external receiver. The implanted unit is powered by an external energizing coil, thus, eliminating problems associated with battery failure. The use of inductive power and telemetry eliminates the need for wires penetrating

The scalp which could provide a pathway for bacteria and lead to infection.

Progress

Competitive proposals for further commercial development of the ICPM system were reviewed in January and a medical device manufacturer was selected. Details of this commercialization process are provided later in this report in the Commercialization Section.

Following the results of successful chronic animal trials with the units fabricated by Konigsberg Instruments, Inc., clinical trials were begun at Stanford University in February (see accompanying news release). In the course of the year a total of 7 patients were monitored for periods ranging from 2-5 days. Indications for monitoring included closed head trauma and management in the ICU following surgery for brain tumor, cyst, or aneurysm. In each case in which it was possible to verify the accuracy of ICP by an alternative method (lumbar puncture, the epidural telemetry technique was shown to provide an accurate reading. There were no complications attributable to the monitoring. Post-explant calibration of the transmitter confirmed performance within specified stability limits.

Figure 2 shows a patient being monitored in the Surgical ICU after brain tumor surgery. In the foreground is the bedside calculator and print-out device which is used to convert the telemetered frequency to ICP and at 5-minute intervals. Figure 3 is a sample computer print-out of mean epidural pressure (EDP) in mm. Hg plotted against time in days. During this time interval the patient is receiving intravenous medications to control intracranial pressure within normal limits. The use of a programmable calculator with the ICPM in the early phases of clinical

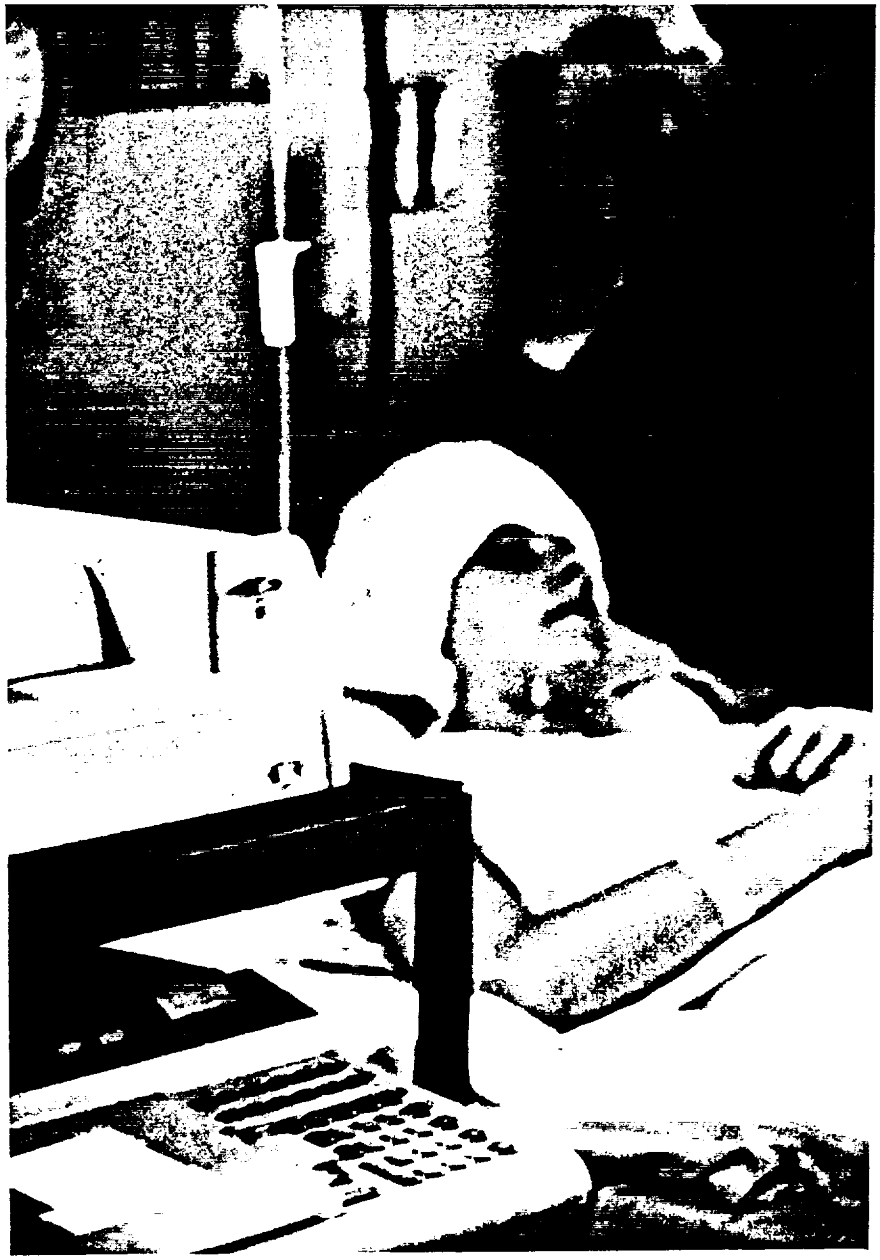


Figure 2: Neurosurgical patient having intracranial pressure monitored in the Intensive Care Unit. Programmable calculator in foreground provides continuous readout. Transmitter energizer and pick-up coil (Fig.1) is hidden by bandages.

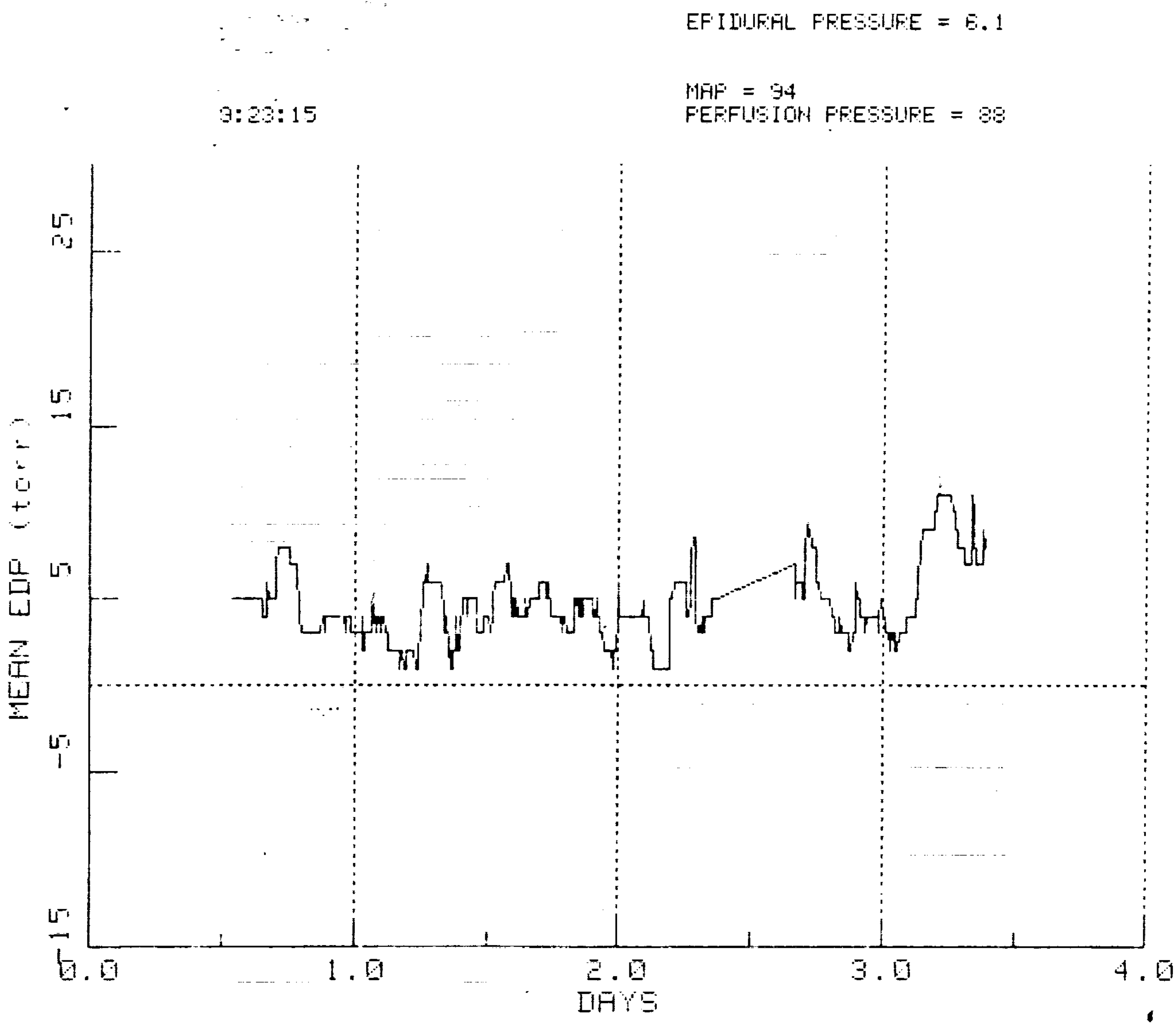


Figure 3: Sample trend plot of mean epidural pressure (intracranial pressure) in mmHg versus time. Record is from comatose, auto accident victim receiving treatment to control ICP.

trials permits great flexibility in data analysis and display of ICP as well as its correlation with othe physiological parameters such as blood pressure, heart rate, PCO_2, and epidural pulse pressure.

At the Fourth International Symposium on Biotelemetry held at Nijmegen University, The Netherlands, Thomas Fryer, the NASA engineer who designed the prototype ICPM, presented a paper describing the electronic circuitry and the results of long-term bench tests. This paper will be published in Biotelemetry IV in early 1979.

At the Thirteenth Annual Meeting of the Association for the Advancement of Medical Instrumentation held in Arlington VA, Dr. Steve Corbin presented a paper entitled "Quantitative Stability Measurements on Implantable Pressure Transducers" which discussed the long-term stability of the ICPM.

In June, Drs. Gene Schmidt and Allen Ream represented the NASA-Stanford ICP Monitoring Group at the "Workshop on Monitoring the Acutely Brain-Injured Patient" held at Wake Forest University, Bowman Gray Medical School, Winston-Salem NC. Drs. Schmidt and Ream made presentations on the ICPM and discussed priorities in patient monitoring and the format for meaningful display of data at the bedside.

In October, representatives of Pacesetter Systems, Inc., NASA-Ames Research Center, and Stanford University Medical School met to review progress on the Pacesetter contract to produce an advanced second-generation ICPM. Pacesetter demonstrated a working model of the transmitter mounting fixture and insertion tool. They also proposed a major revision in the transmitter circuitry to incorporate electronic auto-calibration requiring hybrid circuitry including an LSI chip and programmable read-only memory. Although these changes would require a 6-8 month delay in the delivery date, the consensus of the group was that the suggested improvements were compatible with the goal of a reliable, economical instrument suitable for widespread clinical use.

All ICP measurements made with the implanted epidural transmitter require that the pressure be referenced to ambient atmospheric pressure. In December, a digital electronic manometer was procured to provide this reference pressure. NASA-Ames engineers asssisted in the calibration of this sensitive instrument and it has been installed in the bedside monitoring cart to provide a continuous atmospheric reference.

Plans

Neurosurgical patient implants at Stanford University and bedside monitoring will continue at a rate of 1-2 patients per month using the Konigsberg fabricated units while awaiting the delivery of the new Pacesetter units. A Hewlett-Packard System-45 programmable calculator with extensive graphics capabilities was delivered in November and will be programmed in the spring of 1979 for bedside display of patient data in the Surgical ICU. A site visit to Pacesetter will be held in the spring of 1979 to review progress in the design and fabrication of the second-generation system.

STANFORD UNIVERSITY MEDICAL CENTER
News Bureau Stanford, California 94305

Editors: Photos available if not included with story.

FOR IMMEDIATE RELEASE

STANFORD—

Changes in the pressure of fluid surrounding the brain can now be monitored continuously and noninvasively in humans with a device developed by Stanford physicians and engineers with the National Aeronautics and Space Administration (NASA).

Increases in intracranial, or brain fluid pressure which result from head injuries, tumors, surgery, or fevers can damage the brain and may be fatal.

Early detection and treatment of these pressure rises may prevent brain damage and increase the patient's chance of recovery.

The device, called an intracranial pressure monitor, converts pressure signals into radio waves and relays them to a receiver. The transmission of physiological signals in the form of radio waves is known as biotelemetry.

The first implant of this device in a patient on the West Coast was performed Feb. 16, 1978 by Dr. Gerald Silverberg, assistant professor of surgery at Stanford University Medical Center.

"This is one of the few workable telemetry devices which is accurate and stable," said 'ilverberg.

The patient was a young man who required surgery to remove a brain cyst. Sivlerberg said implanted the monitor because of the risk of the brain swelling and increased fluid around the ..in as a result of the surgery.

The pressure values obtained by the device were checked against spinal fluid pressure .adings. "The values matched extremely well," said Silverberg.

"The surgery worked out beautifully," he said, "and the pressure in the brain did not increase."

The device was removed from the patient after five days. It will be recalibrated, sterilized, and used again in patients who have a high risk of increased intracranial pressure.

In the past, pressure has been measured by inserting a catheter into the brain, a technique that is difficult and can be risky.

The intracranial pressure monitor, on the other hand, provides a safer way of measuring pressure changes without puncturing the membrane which surrounds the brain.

The thimble-sized device is fitted through a 16 millimeter hole drilled in the skull so that it touches the brain membrane but does not pierce it. The device is then covered by the scalp.

Radio signals sent by the device are picked up by an external coil placed above the scalp. After processing by a computer, the signals are displayed on a chart in graphic form.

The device is externally powered by radio frequency waves, eliminating the need for wire connections or batteries.

Arterial blood pressure, blood gases, and heart rate, which are related to intracranial pressure values, are monitored separately.

The intracranial pressure monitor was developed by Thomas fryer, a NASA engineer at the Ames Research Center in Mountain View. Part of the device consists of a transducer used in advanced aircraft and space flight experiments at Ames.

NASA engineers and Stanford physicians have been cooperating in the development of the device as part of the Stanford Biomedical Application Team (BATeam).

The Stanford BATeam is one of four established by NASA in 1966 specifically to transfer aerospace technology to the solution of biomedical problems.

Dr. Donald Harrison, Dr. Eugene Schmidt, and Harry Miller of the division of cardiology direct the BATeam.

Three monitors built by Konigsberg Instruments, Inc., of Pasadena, California, "have performed adequately in long-term bench and animal tests," said Dr. Schmidt,

NON-INVASIVE CARDIOVASCULAR MEASUREMENTS CONFERENCE

Objective

To conduct a major international conference, highlighting NASA technological advances in non-invasive cardiovascular monitoring, and publish an edited text as a result of the presentations and interpretations.

Background

The Stanford BATeam has conducted four major conferences regarding NASA's contributions to the advancement of biomedical instrumentation. They have rpovided a forum for the dissemination of NASA technology to industry, universities, and governmental health agencies. The following texts have been published as a result of these conferences:

1. Biomedical Electrode Technology - Theory and Practice, Sept., 1973
2. Cardiovascular Imaging and Image Processing, July, 1975
3. Biotelemetry III, May, 1976
4. Non-Invasive Cardiovascular Measurements, Sept., 1978 (In press)

The Non-Invasive Cardiovascular Measurements Conference was held at Stanford University on September 11-12, 1978, was cosponsored by NASA-Ames Research Center and the Stanford University School of Medicine (Cardiology Div.), and held in conjunction with the FIFTH ANNUAL COMPUTERS IN CARDIOLOGY CONFERENCE (an international society) who met September 12-14, 1978. Most Computers in Cardiology attendees took advantage of the opportunity to attend the Non-Invasive Cardiovascular Measurements

Conference as well. In addition, a combined session, including speakers from the NASA and Computers in Cardiology group, entitled Nuclear and Computerized Tomographic Imaging was held on September, 12, 1978.

The Conference Planning Committee consisted of:

1. Harold Sandler, M.D.
   Director, Biomedical Research Division
   NASA-Ames Research Center

2. Herb Holley
   Technology Utilization Officer
   NASA-Ames Research Center

3. Donald Harrison, M.D.
   Chief, Cardiology Division
   Stanford University Medical School

4. Gene Schmidt, M.D.
   Assistant Director
   Stanford BATeam

5. Richard Popp. M.D.
   Director, Non-Invasive Cardiovascular Laboratory
   Stanford University Medical School

6. Dhanjoo Ghista, Ph.D.
   Bioengineer
   Palo Alto Veterans Administration Hospital

7. Harry Miller
   Deputy Director
   Stanford BATeam

241 individuals attended the conference representing private practice, academic medicine, engineering, biomedical engineering, computer technology, government, industry, hospitals, universities and private institutes. Attendance was international in scope with 8 different countries represented.

Twenty-one speakers, including a keynote address by C.A. Syvertson, Director of NASA-Ames Research Center, discussed the following topic areas:

1. Echocardiography
2. Blood Pressure
3. Magnetocardiography
4. Radiography
5. Computerized Tomography
6. Flow Perfusion
7. Intravenous Contrast Angiography

Conference Theme

There continues to exist a close evolutionary relationship between the development of computers and non-invasive diagnostic instrumentation. Recent advances in cardiovascular monitoring have been made possible because of parallel advances in microelectronics, computerized signal processing, and algorithms for quantitative measurement and analysis.

It is likewise appropriate that the National Aeronautics and Space Administration (NASA), which provided much of the impetus to develop high speed, low power, microelectronic instrumentation, should support and encourage developments in biomedical applications of this new technology. Through its office of Technology Utilization, its three biomedical applications teams and technology application teams, located throughout the country, NASA is striving to maximize the widespread use of its scientific and engineering knowledge in innovative ways. The impending decade of the space shuttle marks the threshold of a new medical era with increasing reliance on non-invasive imaging and monitoring of patients.

By means of high frequency sound, superconducting magnetic sensors and new methods for coding and decoding x-ray information, physicians are being offered an increasing range of diagnostic tools and techniques for obtaining quantitative information about the status of the cardiovascular system in health and disease. During this conference, representatives of universities, corporations and government had the opportunity to share the discoveries, achievements, successes and failures arising from computer-assisted endeavors to make meaningful and non-traumatic measurements of the cardiovascular system.

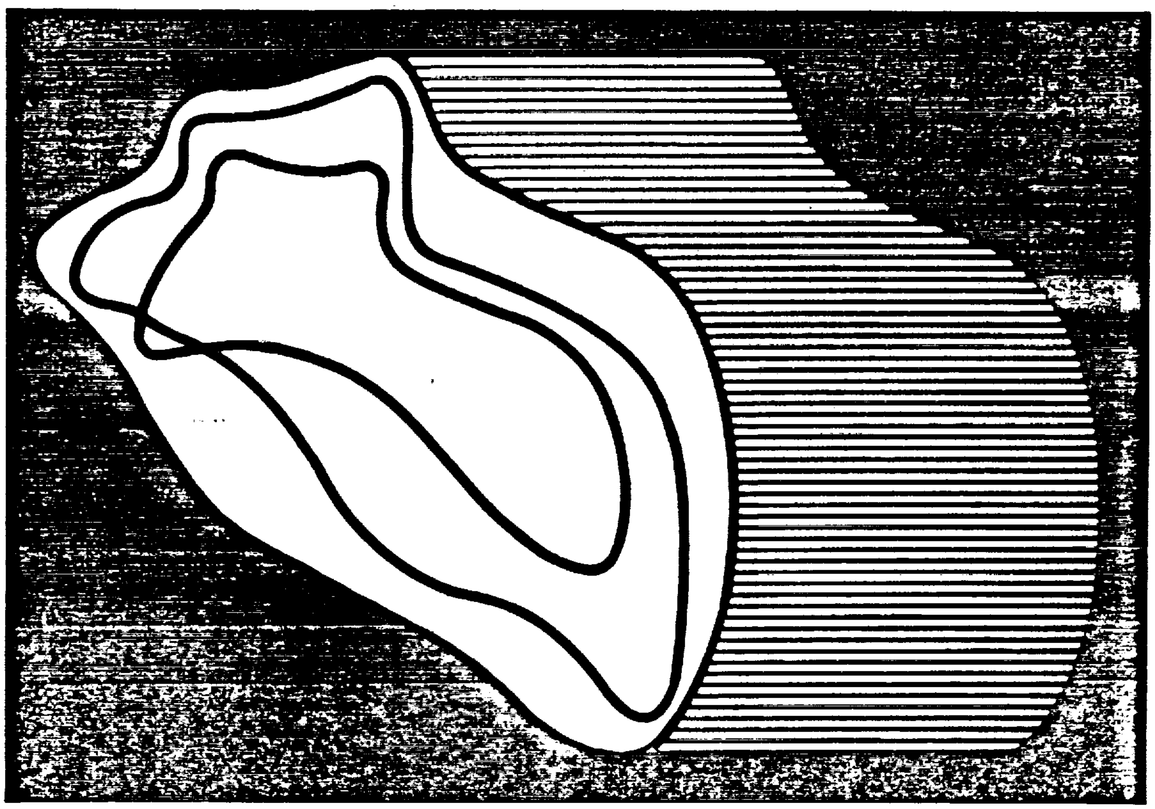
Text

An edited text, as a result of the conference, is in presss and is planned to be released in April, 1979. Each attendee will receive a copy; and a marketing effort for sale to the pbulic, distribution to libraries, universities, and standing orders to a variety of scientific and technological firms is planned by the Society of Photo-optical Instrumentation Engineers (SPIE), who is the publisher.

Editors are Harry Miller, Gene Schmidt, Donald Harrison and Paul Purser. The volume contains 240 pages of new and advanced technology focused on the non-invasive diagnostic measurement of the cardiovascular system. Twenty-one well-known international authorities in the field contributed to the book. The editors have integrated the scientific content into an overview and discussed the economic and regulatory considerations of the technology.

The following are sample cover and title page from the edition. The book will be available in hard- and soft-bound issue.

NONINVASIVE CARDIOVASCULAR MEASUREMENTS



Editors:
Harry A. Miller
Eugene Schmidt, M.D.
Donald C. Harrison, M.D.

SPIE

NONINVASIVE CARDIOVASCULAR MEASUREMENTS

Editors:
Harry A. Miller
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Associate Editor:
Paul E. Purser, P.E.

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Office of Technology Utilization
and
Cardiology Division
Stanford University

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Bellingham, Washington 1978

LIQUID CIRCULATING GARMENTS

Objectives

1. To evaluate research and patient care applications of NASA-developed liquid circulating garments.
2. To assist with transferring this technology to medical device manufacturers so that the garments will be commercially available to hospitals.

Background

The ability to precisely lower or raise patient body temperature is needed for a wide variety of medical applications:

1. Surface cooling has become an accepted alternative and adjunct to cardiopulmonary bypass while performing certain types of open heart surgery (particularly in infants) because a lower body temperature decreases metabolic rate and oxygen consumption.
2. Low body temperatures have a protective effect on patients with diffuse brain injury. Also, in cases involving hypothalamic damage thermoregulatory function can be impaired, resulting in a life-threatening fever--unless exterior cooling is applied. Further research is being done in these neurological areas.
3. Better body temperature controlling methods are needed for patients with fevers caused by infection or brain injury.

Cooling blankets are sometimes inadequate because they do not provide sufficient body surface contact for heat exchange, lack sufficiently precise temperature control, and are prone to mechanical failure.

4. Pre-cooling patients with muscle spasticity caused by multiple sclerosis appears to allow them to exercise more adequately during physical therapy. At present, pre-cooling requires that a patient be immersed in 60° Fahrenheit water. Liquid-cooled suits may eliminate the inconvenience and discomfort involved in this procedure.

5. Two patients, each having a rare disease, have benefited from the use of surface cooling with custom-designed cooling garments:

   A. A boy who has hyperkeratosis (a congenital disease which results in skin thickening and subsequent loss of normal heat-loss mechanisms) was able to move about comfortably only with externally applied cooling via a custom-fitted NASA suit.

   B. A girl who has "burning limb syndrome: (a congenital condition which causes severe pain in the limbs) gained marked relief when her limbs were cooled continuously with a specially-tailored, liquid-cooled garment.

   Previous cooling methods involved application of wet packs. Such applications caused problems in these two cases. Wet packs were too cumbersome to allow needed exercise for the boy. In the girl's case, the constant use of cold water showers caused skin irritation and ulceration which eventually led to bilateral amputation of the legs.

6. One unproven, but promising, approach to the treatment of metastatic cancer is to elevate the patient's body temperature. This treatment, alone and in conjunction with chemotherapy, is being investigated. Various methods of raising and maintaining

supranormal body temperatures, including the NASA liquid circulating garment, are under investigation by the National Cancer Institute.

7. Detection of breast cancer may be possible if the surface temperature over a tumor is higher than the normal breast surface temperature. One noninvasive way to measure this is to scan the breasts with a detector sensitive to heat emissions (infrared radiation). This technique is known as thermography.

Breast pre-cooling results in a uniform initial temperature and more contrast in the ensuing thermographic scan. Differences between transient re-warming characteristics of healthy versus abnormal breast tissue may indicate suspected cancer more

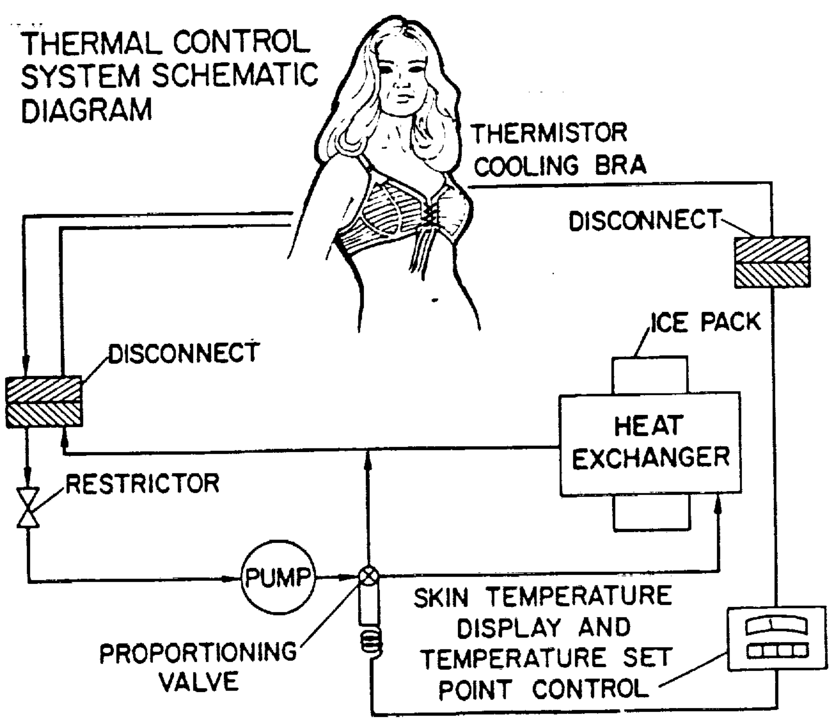


FIGURE 1

accurately if the breasts are uniformly cooled prior to the thermographic examination.

A specially-designed liquid-cooled brassiere (Figure 1) is being evaluated for this application.

8. Because fetal thermoregulation is developed late in gestation, neonates do not have adequate body temperature control. A convenient method to control infant body temperature is needed.

NASA Technology

Liquid circulating garments were originally developed by NASA-Ames Research Center to protect astronauts from adverse thermal effects during extra-vehicular excursions. These garments have been improved so that their heat transfer panels are not only more flexible, but they are also held snugly against the body by elasticity which has been built into the garment. The panels consist of a flexible polymer which contains tiny channels through which cooled or heated water is circulated. Modifications of the aerospace suit have been made in order to produce a garment suitable for operating room and clinical treatments (Figure 2).

Several customized garments have been made at Ames: Cooling vest (for patients with hyperkeratosis), bermuda shorts (for the double-amputee, "burning limb syndrome" patient), and infant garments.

Shipment of garments, each with an associated pump and control cart, recently began. The recipients qualified for the garments by submitting a protocol, which included approval by the investigator's individual Human Subjects Research Committee. Documented follow-up of program status, problems, and success rates has been assigned to the nearest BATeam.

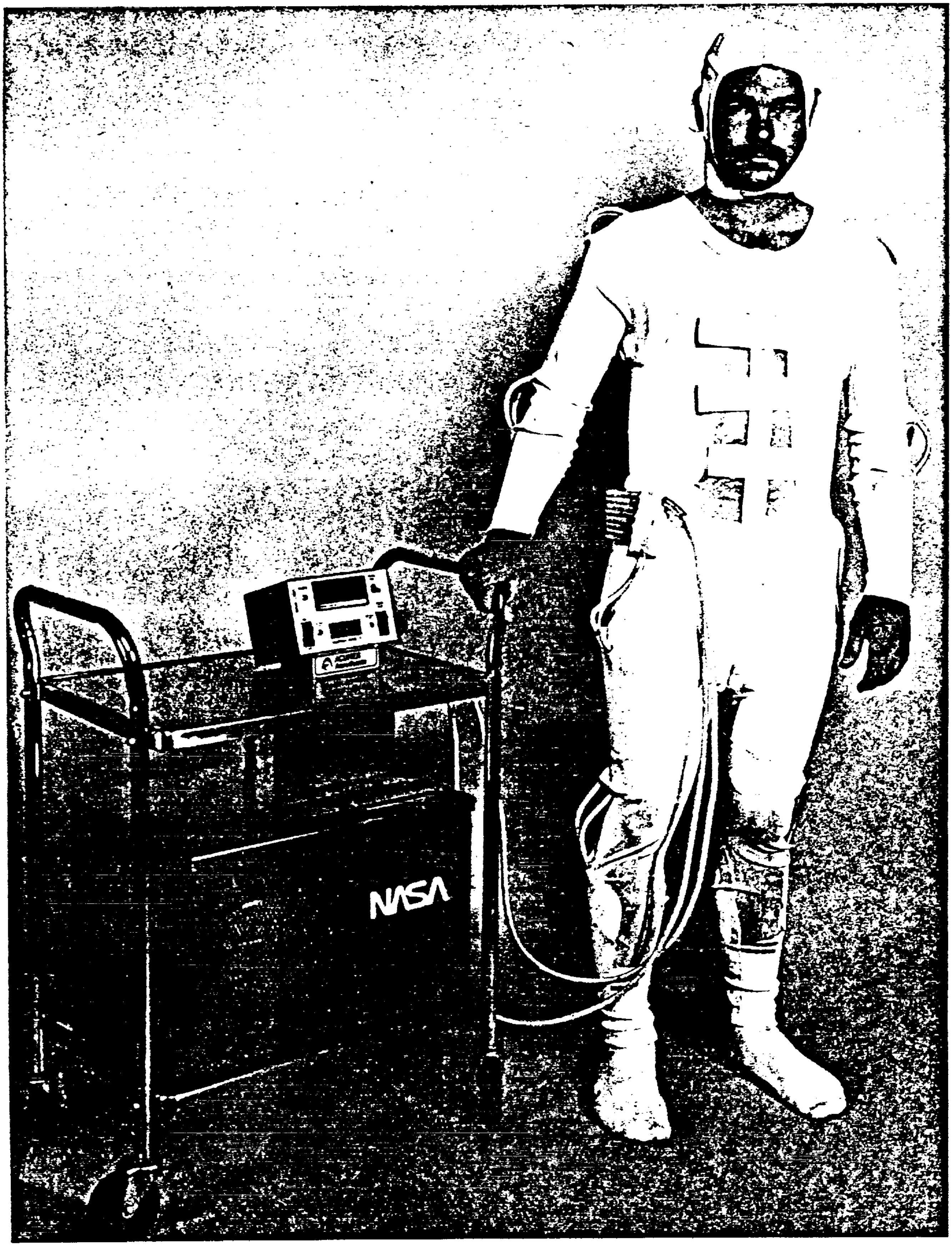


FIGURE 2
Full-Body Liquid Circulating Garment and Thermal Control Cart

The following investigators, listed by their medical specialties, are receiving NASA liquid circulating, temperature control equipment:

1. Whole Body Hypothermia

   *Gerald D. Silverberg, M.D.
   Neurosurgery Department
   Stanford University School of Medicine
   Stanford, California

   *Allen K. Ream, M.D.
   Anesthesiology Department
   Stanford University School of Medicine
   Stanford, California

2. Whole Body Cooling - Treatment of Multiple Sclerosis Symptoms

   *Colin Bamford, M.D. and William Sibley, M.D.
   Neurology Department
   University of Arizona
   Tucson, Arizona

   Floyd A. Davis
   Multiple Sclerosis Center
   Presbyterian-St. Luke's Hospital
   Chicago, Illinois

3. Cooling - Treatment of Hyperkeratosis Symptoms

   O. Fred Miller, M.D.
   Dermatology Department
   Geisinger Medical Center
   Danville, Pennsylvania

4. Cooling - Relief of "Burning Limb" Syndrome Symptoms

   Walter H. Johnson, Ph.D. and George Hahn, M.D.
   Crippled Children's Hospital
   Toronto, Ontario, Canada

5. Whole Body Hyperthermia - Treatment of Metastatic Cancer

   *Jerome Block, M.D.
   Harbor General Hospital
   Torrance, California

   David Van Echo, M.D.
   National Cancer Research Center
   National Cancer Institute
   Baltimore, Maryland

* *Investigators whose progress is being monitored by the Stanford BATeam.*

James Larkin, M.D.
University of New Mexico Medical Center
Albuquerque, New Mexico

6. Breast Cooling - To Aid in Possible Breast Cancer Detection

*James Vaudagna, M.D.
Radiology Department
Good Samaritan Hospital
Los Gatos, California

7. Thermal Control of Neonates

Ernest N. Kraybill, M.D.
Pediatrics Department
School of Medicine
University of North Carolina
Chapel Hill, North Carolina

Progress

During this reporting period liquid circulating carts and garments were checked out and shipped from the NASA-Ames Research Center to Drs. Block, Davis, Atkinson, and Kraybill for various evaluations as listed previously. One of the more promising applications of this technology has been under evaluation at the National Cancer Institute in the treatment of patients with metastatic cancer. As reported in the May. 29, 1978 issue of Medical World News, preliminary results have shown that hyperthermia can be safely administered when the patient is carefully monitored. Fourteen patients with a variety of metastic malignancies were tested at the NCI and four of them showed measurable tumor shrinkage after body temperatures had been raised to 41.8°C. for up to 4 hours. A number of different liquid circulating garments and temperature control carts are being used in this study; one of them was provide by NASA. The NCI investigators are conducting studies to rule out any damage to the cardiovascular system as a result of the elevated body temperatures required. Although four of fourteen patients showed some improvement following hyperthermia treatment, these results must be considered preliminary at this time.

On March 21, 1978 the Stanford BATeam participated in discussions with representatives of the American Hospital Supply Corporation. The meeting was held at the Ames Research Center under the direction of Herb Holley, TUO. Potential medical applications in both hyper- and hypothermia were discussed. Mr. Paul Tramell, Director of Applied Research for American Hospital, expressed particular interest in manufacturing a disposable garment for various pediatric applications. Dr. James Brown, Director of the RTI Biomedical Team, will follow up evaluation of this potential application with American Hospital in collaboration with the University of North Carolina Medical School Pediatrics Department.

There have been several delays in obtaining a suitable system for neurosurgical applications of full-body hypothermia. Several modifications of the standard NASA garment depicted in Figure 2 have been made to facilitate its use with the comotose patient. Since the patient would be lying on his back much of the time, the suit has been reversed so that the tubing and manifolds come out the front. The suit is split down the front and along the inseams of the legs, and Velcro fasteners have been added to facilitate suiting up the patient. The sleeves have been shortened to permit access to the arms for IVs and drawing blood specimens. Likewise, the groin area is accessible for drawing blood gases and waste management. The cart and garment delivered by Acurex will require midifications before it can be used in the hospital setting. One of the cooling panels will have to be replaced because of leakage; the interjoint tubing, which tends to kink and obstruct the free flow of circulating liquid, will be replaced by stronger preformed urethane tubing. The cart was found to exceed the hospital safety limits for leakage current and an isolation transformer has been installed to correct this problem.

Evaluation of the liquid-cooled bra for enhancement of breast thermography has begun but progress has been slow. Studies in the first half of the year were delayed by a mechanical failure in the thermography camera which required installation of a new infra-red detector. Of the first six patients evaluated, one had confirmed breast cancer. In this patient the standard room temperature thermogram gave equivocal results; however, the cooled-bra thermogram was markedly abnormal, showing early revascularization of the breast with the tumor. Based on this promising early result, Dr. Vaudagna, the radiologist conducting this evaluation, was encouraged to perform cooled bra examinations on additional cancer patients. However, the personal physician or surgeon of patients already diagnosed as having breast cancer have been reluctant to refer them for any additional test which might create a delay in their receiving appropriate therapy. By the end of the year, a total of 15 patients had received both standard thermograms and cooled bra thermograms. Five of the 15 patients had previously-confirmed malignant lesions. In one of these 5 the thermogram could not be recorded due to technical difficulties. In 2 of the 4 remaining cases of confirmed breast cancer, the cooling procedure provided marked enhancement or contrast in the thermogram and the breast with the lesion was easily identified. Though these numbers are far too small to be statistically significant, the radiologist would like to continue the evaluation including a larger number of patients with confirmed breast cancer.

Dr. Jerome Block, UCLA Harbor General Hospital, has only recently begun his investigations of full-body hyperthermia in the treatment of metastatic cancer using the standard NASA liquid-circulating garment. He reports that more flexibility in adjusting the size of the suit is desirable; patients with large chest tumors frequently have a large abdominal girth and thin arms and legs., making it difficult to achieve a snug fit. Also, the placement of the manifolds on the back of the suit makes it somewhat uncomfortable for the patient to lie down. Although his investigations are just beginning, Dr. Block has stated that the patient acceptance of the garment has been good.

Plans

The manufacturer, Acurex, is proceeding with the indicated modifications in the garment for use by Dr. Silverberg. They are also fabricating temperature control carts with redundant temperature-sensing circuitry which will meet hospital leakage current standards. Once the modifications of the suit are completed, the BATeam will conduct a 48-72 hour simulated life test before releasing the equipment for patient applications.

Reports from the University of California Medical Center (San Francisco) and Stanford University have shown that whole-body hypothermia (cooling to 31°C.) may be helpful in reducing brain damage in pediatric drowning victims. The BATeam will contact physicians at these institutions to determine if the NASA LCG is applicable.

VERSATILE PORTABLE SPEECH PROSTHESIS

Objective

Incorporate NASA communications technology into the development of an electronic versatile portable speech prosthesis (VPSP) for the efficient production of highly intelligible synthesized speech by physically handicapped, non-vocal patients.

Background

There are approximately 1,500,000 non-vocal people in the United States who need communicative assistance for educational, vocational, and social purposes. This figure includes patients suffering from cerebral palsy, multiple sclerosis, Parkinson's disease, muscular dystrophy, stroke (with residual aphasia), and cancer of the larynx (post-laryngectomy patients). These people cover a wide range of age groups and all share the problem of being unable to speak. Many may not be able to use their hands for writing, typing, or sign language - in essence, these patients have no means of communicating.

In order to provide for a flexible speech communicator and rectify the variety of problems and limitations plaguing current communication aids, the following design goals were proposed:

1. Minimize the requisite training period needed to achieve proficient use of the device.

2. Provide for easily-implemented, user-initiated vocabulary expansion.
3. Configure system to be adaptable to a wide range of user disabilities.
4. Optimize system for rapid sentence construction and improved speech intelligibility.

NASA Technology

The VPSP makes extensive use of aeronautical communications technology, developed by the Manned-Vehicle Systems Research Division of NASA-Ames Research Center. NASA Flight Management personnel are investigating the use of synthesized speech for advanced aircraft communications.

Experimental systems have been developed to provide synthesized voice readout of aircraft altitude, air speed, sink rate, and deviation from desired flight paths as an aid to pilots during critical aircraft malfunctions.

The NASA speech system consists of a powerful message editing software package and a system of phonetic contextual and intonation rules, developed by Dr. Carol Simpson. Research has been conducted to improve intelligibility, comprehension ease, situational appropriateness, and system flexibility over a wide range of flight contexts.

These principles and approaches are directly applicable to the VPSP. In particular, the rules for modifying phrasing, intonation, and phonetic structure will be used to maximize intelligibility of the VPSP's synthetic speech output.

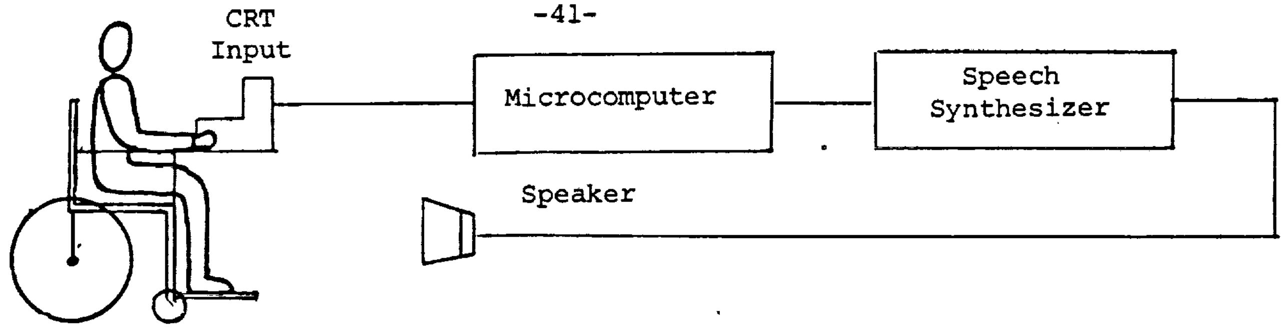


Figure 1A: Primary System Components (All components packaged onto wheelchair)

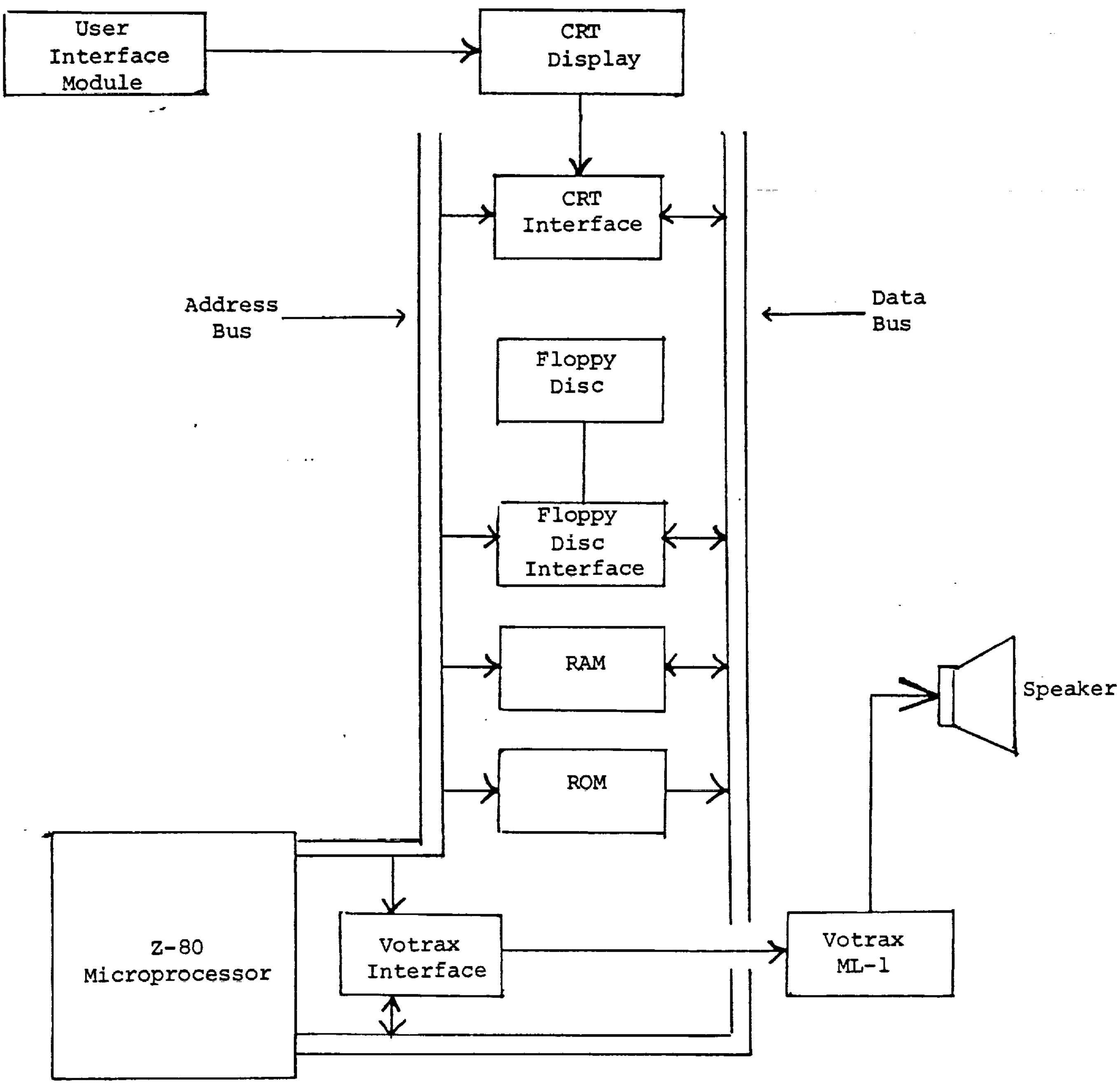


Figure 1B: Hardware Elements

Approach and Progress

Substantial progress has been realized at both hardware and software levels during this past year. The project design goals have been closely adhered to and an April 1979 demonstration of the VPSP to NASA representatives is anticipated.

The major components of hardware used in the project are: 1) Z-80 microprocessor, 2) floppy disc memory, 3) on-board ROM and RAM, 4) Votrax ML-1 speech synthesizer, and 5) CRT coupled to User Interface Module. This system is diagrammatically presented in Figure 1.

The User Interface Module (UIM) represents that element which transduces the residual interactive capability of the nonvocal individual into electric signals which can be utilized in sentence composition on the CRT screen. Some possible UIMs are given in Table 1.

This VPSP prototype is being developed assuming a "worst-case" individual, i.e. a person who could actuate only a simple on-off switch such as a sip-n-puff tube. Solving this problem makes interfacing with a more advanced UIM that much easier.

This microcomputer-based system will be powered by the same battery that drives the wheelchair.

The software can be functionally divided into four modules; 1) Page layout, 2) CRT input and editing, 3) Text-to-phoneme decomposition, and 4) output driver routines for the speech synthesizer (as outlined in Figure 2).

The layout of words on the CRT screen (page) and the further organization

TYPE	CAPABILITY
Binary Switch (i.e. sip-n-puff tube)	User starts and stops auto menu scan to select word.
X-Y Controller (i.e. Joy-stick)	User moves cursor directly to desirable word.
Teletype	User section and text composition directly from keyboard.

Table 1: Typical User Interface Modules

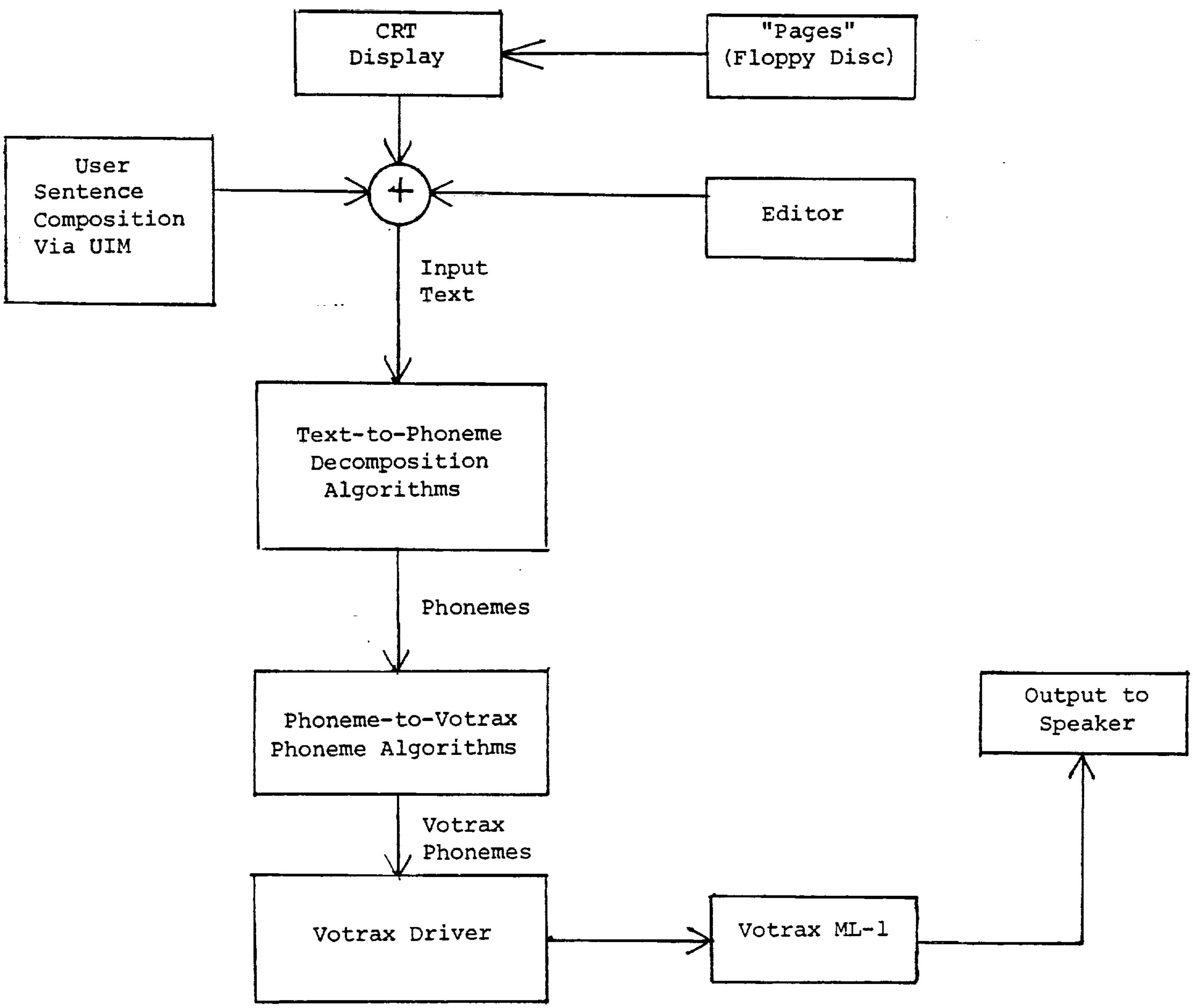


Figure 2: Software elements

of these pages are two important parameters which govern the speed of sentence construction. Through experimentation, Dr. Carol Simpson has found that a page display formated in a syntactic pattern with alphabetical ordering of the words is the most efficient in reducing the time required for message construction. An example of this type of layout is shown in Figure 3.

Through use of the Input/Editing routine, the user can modify or correct sentence construction before it is processed by the text-to-phoneme module. The text is decomposed by the application of phonemic and intonation algorithms and the resulting digital code is used to drive the synthesizer to produce speech.

Each CRT page will be stored in a block of floppy disc memory, which enables the user rapid access to a desired page.

Commercial interest in the VPSP is very keen. Some current proposals are:

1. Votrax (a division of Federal Screw Works), which has donated two ML-1 speech synthesizing units (approx. $40K) to the project, is very much interested in manufacturing and marketing possibilities of the VPSP.
2. Telesensory Systems, Inc. is interested in exploring the possibilities of mating the VPSP with their Autocom units, thus replacing the CRT and making the system more portable and flexible.

In summary, the VPSP is both commercially attractive and promises to be an important development in the field of rehabilitative communications aids.

HOW	ARE	HE	BUY
HOW MUCH	CAN	I	COME
WHAT	COULD	IT	DO
WHEN	DID	SHE	EAT
WHERE	DO	THEY	GET
WHICH	DOES	WE	GO
WHO	HAS	YOU	KNOW
WHOM	HAVE		LIKE
WHOSE	IS		MAKE
WHY	SHOULD		PAY
	WERE		READ
	WILL		SAY
	WOULD		SEE
			WANT
			WATCH

Figure 3 - Syntactic/Alphabetic Page Layout

Plans

As a result of hardware contributions by Votrax the further development of the VPSP will be divided into two concurrent phases. The first phase will involve the packaging of the Z-80 microcomputer-based system. This will be integrated into a battery-powered wheelchair and will undergo subsequent patient trials and evaluation during the summer of '79.

A second phase system, based on the SOL-20 microcomputer from Processor Technology, will be used for further software development and refinement. The resulting software improvements will be incorporated into the phase I system. Additional NASA funding (1980 RTOP) will be sought for continuation of this phase.

PURKINKE IMAGE EYETRACKER

Objective

Redesign the SRI (Stanford Research Institute, Menlo Park, CA) Image Eyetracker in order to provide an economical clinical instrument for the quantitative measurement of eye motion disorders associated with neurological diseases, such as multiple sclerosis.

NASA Technology

The SRI Purkinje Image Eyetracker is the result of an effort, begun at SRI during the 1960s, by Doctors Hew Crane and Tom Cornsweet in collaboration with Ames Research Center. The initial goal was to develop an instrument which would provide high resolution real time data for studying the visual performance of pilots; that is, to study their tracking and scanning patterns of near instrument panels and far fields and their ability to focus (accommodate) in the presence of light or dark backgrounds.

Background

The oculomotor system requires integration of cerebral, cerebellar, and brainstem pathways to function properly. Thus, accurate observation of eye movements can provide a sensitive monitor for neurological dysfunction. To date, classification of ocular movement disorders has been based primarily on descriptive observations.

However, recent eye movement recording and quantification has improved

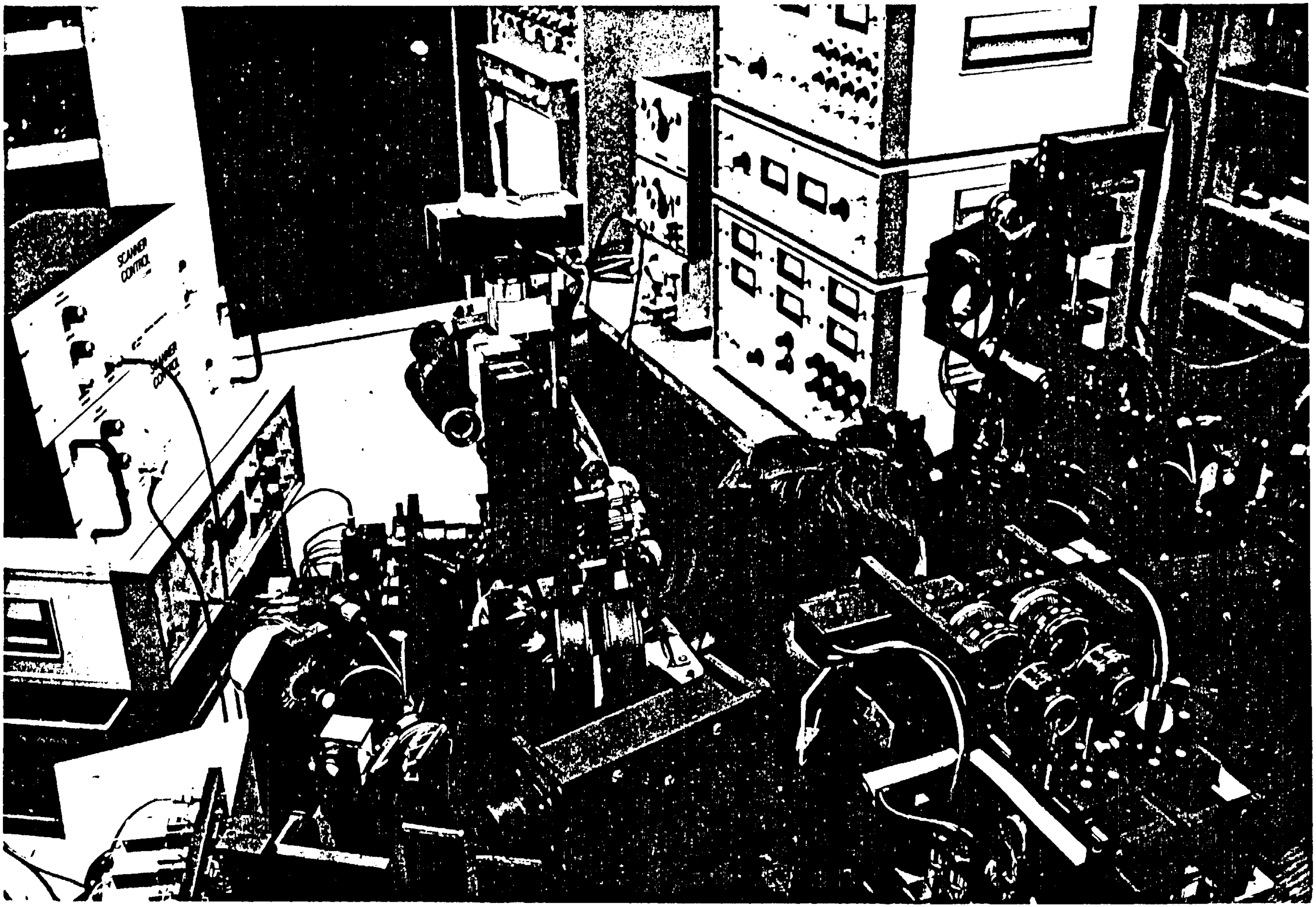


FIGURE 1
BINOCULAR SRI PURKINJE IMAGE EYETRACKER

the understanding of normal ocular physiology and helped identify several characteristics of specific eye movement abnormalities. Knowledge concerning the physiology of pathologic eye movements is largely lacking.

Clinical eyetracker studies have been limited, but promising. Most pathological eye movement reports are based on preliminary studies and evaluate mainly the saccade response and nystagmus. A limiting factor for widespread clinical application of these eye movement studies has been instrumentation.

The Purkinje Image Eyetracker follows the reflections of a point of light which is formed by the front surface of the cornea and the rear surface of the lens. The present system is able to track the relative spatial orientation of these reflections in order to provide data on eye rotation, the direction of gaze (the eyetracker), and a continuous measurement of accommodation (the optometer).

Combining two complete systems (one for each eye) of an eyetracker and optometer yields a new instrument, a three-dimensional eyetracker which gives a continuous measurement of the point in three-dimensional space at which the subject is looking. The fourth generation system can provide data on three-dimensional binocular function, with one minute of arc resolution and a bandwidth greater than 200 Hz.

The optometer portion of the system (distinct from the eyetracker function) was successfully spun off in the early 1970s and is the basis for an automatic refraction measurement system, i.e. automatic determination of a patient's eyeglass prescription, presently manufactured and marketed by Acuity Systems, Inc. (McLean, VA).

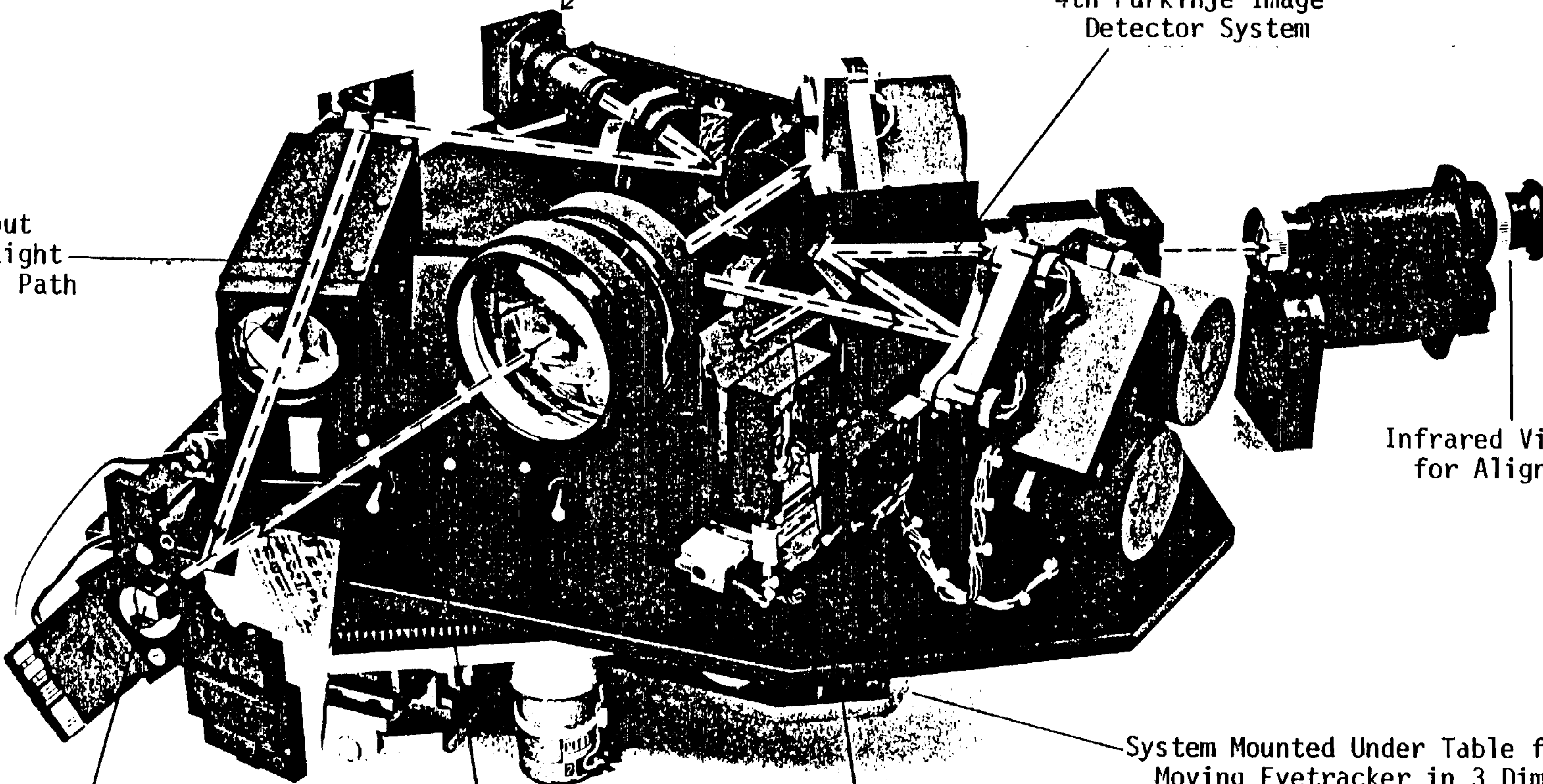


Figure 2.

<u>NEW MONOCULAR PURKINJE IMAGE EYETRACKER</u>: The new optical platform with high speed servoes and driven substage for automatic alignment is less complex than earlier models. The assembly at the lower left is a model eye used during checkout and alignment and is readily removed for

The Purkinje Eyetracker is quite attractive clinically because it not only provides higher resolution than other techniques (such as those using contact lens, eye coils, and electrodes), but being non-contacting, it greatly facilitates patient examination.

The present design is the result of over ten years of development effort and is too complex for mass production. In order to provide for maximum flexibility during the development stage (while new components were being added), all of the twenty optical elements were placed in adjustable mounts (Figure 1). This has contributed to a very extensive, time consuming alignment process. In redesigning this system for clinical use, SRI has simplified the optics and electronics while, at the same time, providing greater eye relief and head freedom to facilitate interfacing with the patient (Figure 2).

While a number of disorders severely compromise the eye's ability to focus on and track an object, the available instruments for studying and quantifying these phenomena are limited. By precisely tracking the spatial relationship of the refelctions of a point source of light from the front of the cornea and the back of the lens of the eye, the SRI International Purkinje Image Eyetracker is able to measure vertical and horizontal motion to 1 minute of arc at up to 200 cycles per second. This high frequency response and resolution makes it possible to see very small, high speed movements, known as micro-saccades, which seem to be affected by various disease processes. When coupled with the appropriate optical and electromechanical systems, the eyetracker can also be used to provide a stationary, stabilized image of the retina which has significant clinical and research potential for studying and treating a variety of degenerative diseases.

Progress

The primary purpose of the present effort is to redesign the system making it simpler, more reliable, and easier to maintain so that its use would be feasible in clinical as well as research environments.

Three clinical studies were initiated in the summer of 1978 by John Hotson, M.D., Stanford University neurologist. The studies used the extreme sensitivity and both the vertical and horizontal components of the eyetracker recordings to observe miniature eye movements during fixation. Previous investigators have identified both "microsaccades" and slow drift movements during fixation. The two main goals were to determine:

1) If these normal fixation movements evolve to produce pathological fixation instability in neurological disorders.
2) If abnormalities of fixation could be used to improve the sensitivity and accuracy of clinical diagnosis.

In approaching this problem the extent of variations from normal fixation in 12 control subjects were found to be considerable. Not only are there microsaccades and slow drift in the miniature movements of fixation, but the substrate for most types of pathological fixation also occurs. Horizontally-coupled saccades (characteristic of square wave jerks); biphasic and triphasic saccades without an inter-saccade interval (similar to ocular flutter); random vertical, oblique, and horizontal saccades (reminiscent of opsoclonus polyphasic square wave oscillations); and vertical nystagmus all occur in control subjects when staring at a target straight in front of them.

The second project involved recording fixation movements in three patients with spinocerebellar degeneration and fixation instability. All of these patients had fixation eye movements of a similar qualitative appearance and frequency but with an amplitude 3-4 times greater than control subjects. At the same time, there was a total absence of horizontal microsaccades. These findings suggest that some forms of fixation instability may evolve from microsaccades whose amplitude has increased due to a loss of cerebellar "gain control." These observations may also indicate that the absence of microsaccades is a new quantifiable diagnostic sign of a bilateral cerebellar disease.

The third project initially sought to determine if abnormalities of fixation occurred in multiple sclerosis, thereby providing a new, sensitive, and quantitative diagnostic tool. The eye movements of five patients with multiple sclerosis without clinical evidence of fixation instability were studied. The eyetracker recordings in three patients were similar to control subjects. Two patients had horizontal and/or vertical nystagmus overriding the eye recordings which obscured non-nystagmoid fixation eye movements. Subclinical nystagmus in multiple sclerosis has previously been reported using less refined recording techniques.

Plans

Over the next year the following consecutive goals have been outlined:

1) Complete the quantification of the eye movement recordings obtained to date and present the results at the American Neurological Association Meeting in the fall of 1979.

2) Make additional recordings of control subjects and patients with cerebellar disorders.
3) Obtain funding to establish at the Santa Clara Valley Medical Center a clinical research eye movement laboratory centered around the Purkinje Image Eyetracker.
4) Once the laboratory is established, continue to pursue the study of fixation eye movements using three main approaches.
   a) Correlations between neuroanatomic structure and function.
   b) Study of the relation between slow drift and pursuit eye movements in control subjects and neurological patients.
   c) Further definition of pathological fixation in neuro-ophthalmological disorders.

There have extensive discussions on coupling an eyetracker-stabilized visual system, to a laser photocoagulator to facilitate treatment of diabetic retinopathy. Technically, this approach is highly feasible. In the coming year, additional clinical trials of the eyetracker will be performed following completion of the new, less complex instrument. Efforts to integrate an eyetracker and photocoagulator will be pursued.

NANOPHOR

Background

Electrophoresis is a laboratory technique for physically separating and identifying serum proteins using an electric field. Serum proteins vary in size, shape, density, and electrical charge so that they migrate at different rates when a suitable electric field is applied. Electrophoresis has been in use for many years relative to both clinical and forensic medicine.

NASA Technology

Benjamin Grunbaum, Ph.D., a University of California biochemist, has invented and developed new electrophoresis instrumentation and techniques. His work has been partially funded by NASA for the development of electrophoretic techniques used to analyze Apollo astronaut serum proteins.

Dr. Grunbaum recently invented a new device designated the NANOPHOR ("nano" specifying a very small quantity and "phor" from the term "electrophoresis").

Background

The NANOPHOR is a versatile analytical assembly for microelectrophoresis and associated technologies. It quickly and economically makes a discrete separation of specific proteins in nanoliter to microliter quantities of blood, thus permitting their subsequent identification and quantifivation. Both a diagnostic and research instrument, the NANOPHOR

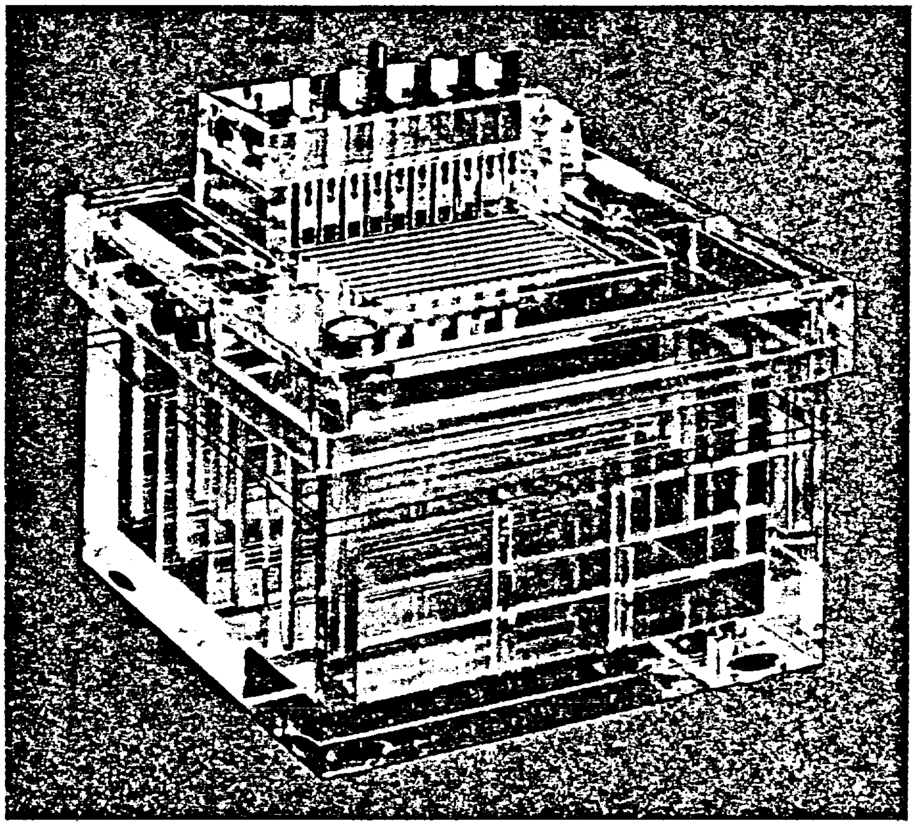


Figure 1. An **Improved Electrophoresis Apparatus** incorporates a multiple-sample applicator and several other new features that both speed up analysis and improve accuracy.

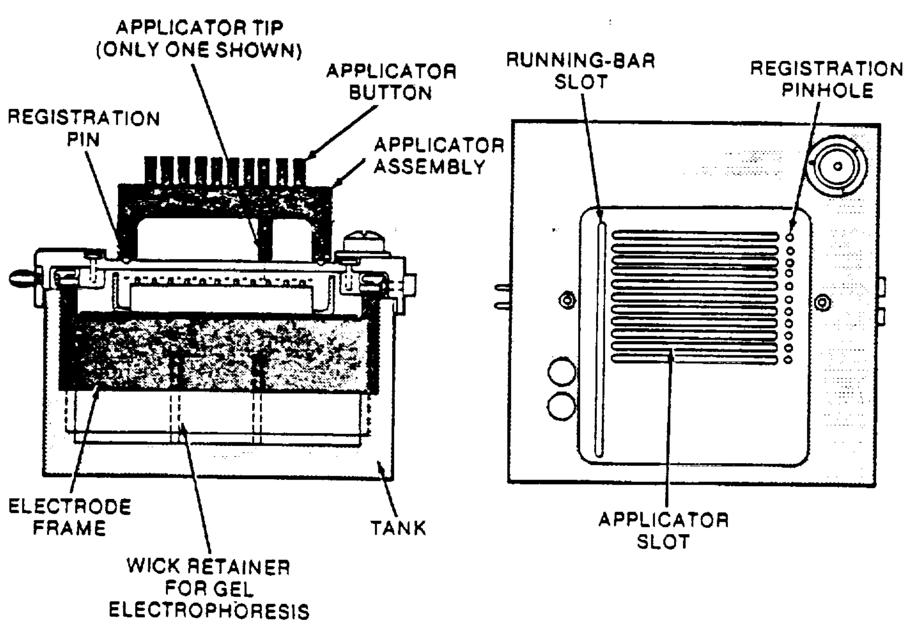


Figure 2. The **Automatic Multiple-Sample Applicator** is shown as used with a specially-designed membrane-medium electrophoresis device. The registration pin is inserted into 1 of 11 pinholes in the cover, and when the middle applicator button is pushed, all 10 applicator tips pass through the slots and release their samples simultaneously.

holds much promise for use in future research and for applications in medicine, immunology, genetics, biochemistry, forensic science, and other biological sciences.

The NANOPHOR is a integrated system of instruments, parts, and accessories designed for use with either cellulose acetate membrane or gel substrates. The basic unit of the system is an electrolyte tank and cover. This unit accomodates either the specially designed, membrane-tensioning bridge or the temperature-controlled plate and gel tray. Included in the system is a multiple-sample holder and a multiple-sample applicator. Used in conjunction with a unique indexing device on the top of the tank cover, the multiple-sample applicator can accurately transfer specimens either simultaneously or individually from the sample holder to predetermined positions on the substrate (Figures 1 & 2).

Progress and Plans

Progress and plans for commercialization of this new medical laboratory instrument are covered in the Commercialization Section of this report.

SPATIAL FREQUENCY MULTIPLEXING

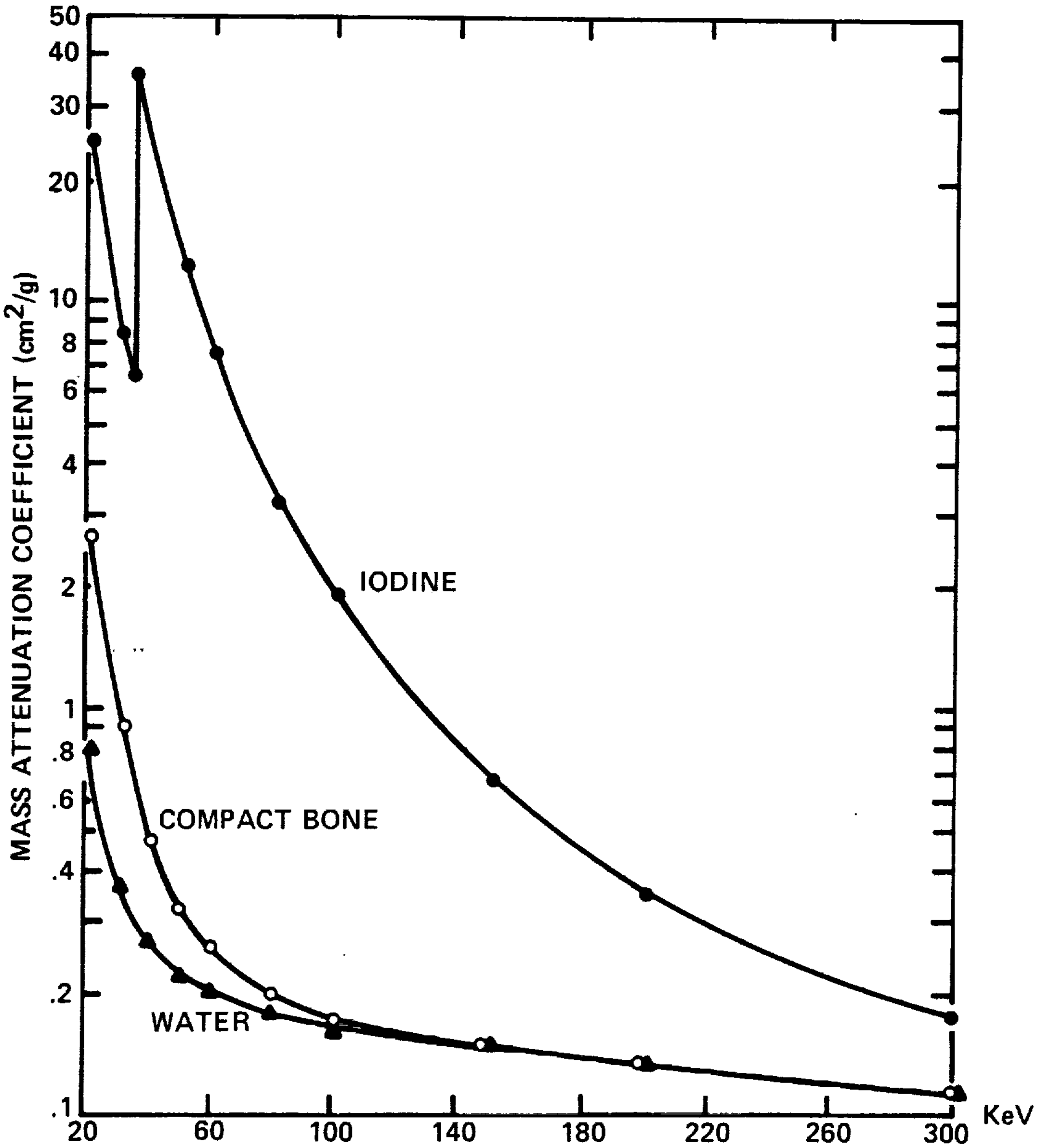
Objective

To apply NASA technology to an x-ray spectral filtering technique which, using commercially available x-ray sources, produces high contrast radiographs of internal organs, soft tissues, lesions, and blood vessels which are beyond the imaging threshold of standard x-ray techniques.

Background

Present radiographs are transmission records of a continuous spectrum of x-rays passing through the body. The transmission of any one photon in the spectrum is a function both of the photon's energy and of the absorption coefficient of the matter through which it passes. Therefore, the standard radiograph is a complex record with both energy and absorption coefficient integrated over a broad spectrum so that subtle differences are lost. For example, substances having components of higher atomic number (of high-Z) absorb a great deal more of the continuous spectrum than does soft tissue; therefore, lung tumors may be hidden by overlying ribs, or metastatic bone cancer may be obscured until the lesions are large and widespread.

Radiologists inject a solution of organically-tagged iodine into the patient's blood stream so that organs which preferentially take up iodine, such as the kidneys, can be radiologically delineated. Yet there is always a trade-off between adequate visualization and toxicity.



ATTENUATION COEFFICIENT vs X-RAY ENERGY

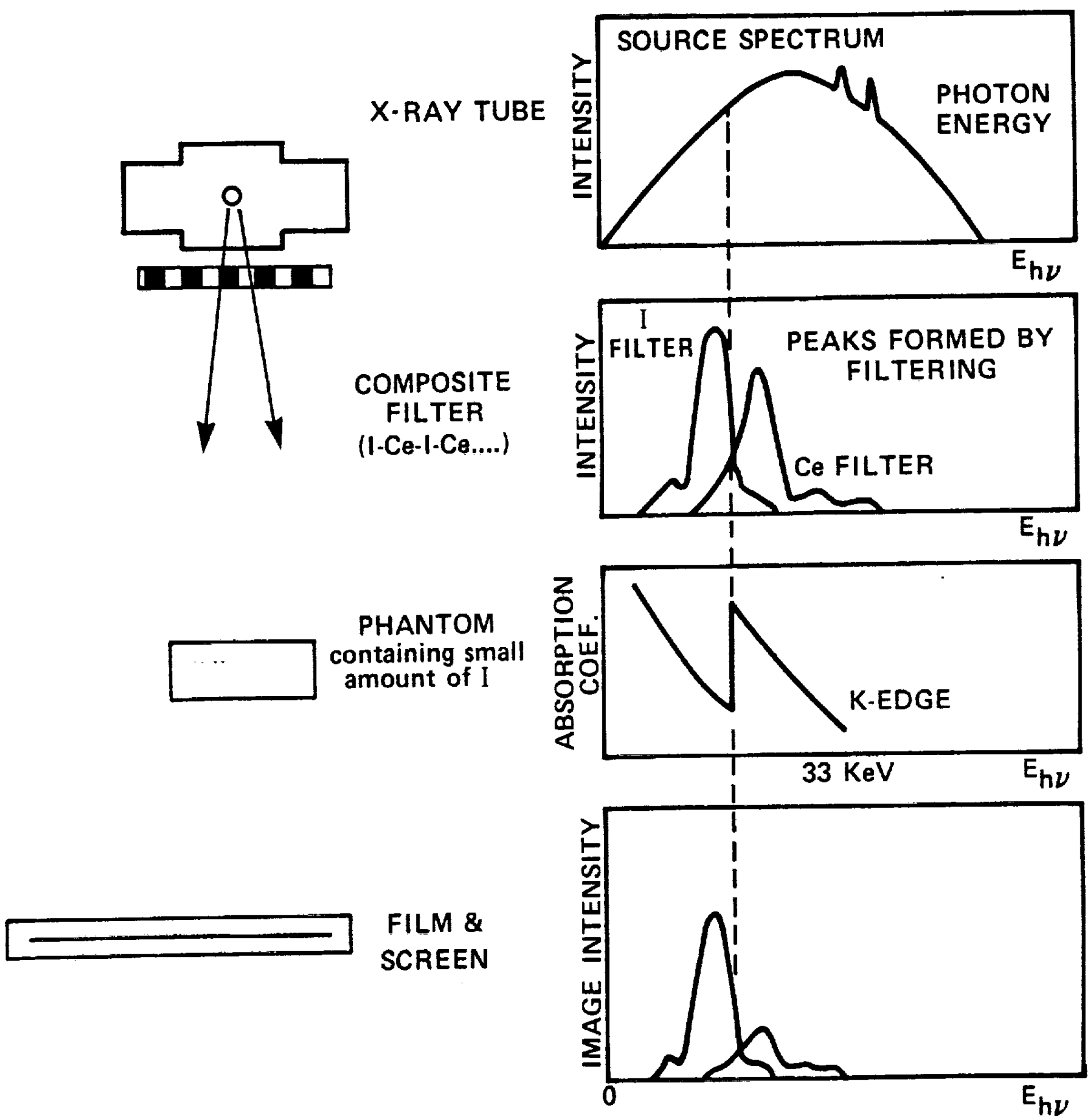
Figure 1

Other organs, such as liver and spleen, would, however, require the injection of toxic doses for adequate visualization. If the sensitivity of iodine detection could be considerably enhanced, these organs might similarly be visualized; and this would, indeed, give the radiologist a new diagnostic tool. In summary, an increase in the sensitivity of iodine detection and a new way to separate soft tissue from overlying bone would provide powerful tools not only to make more accurate and earlier diagnoses but also to diagnose a larger number of diseases.

Approach

Toward these goals, Professor Albert Macovski and his colleagues at Stanford University are developing several promising techniques which cleverly exploit the mechanisms by which tissue, bone, and iodine absorb x-rays. Figure 1 shows the absorption coefficient of these materials as a function of the energy of the individual x-ray photon. Three techniques will be described essentially as they were developed.

The first technique exploits the fact that the absorption of iodine undergoes a sharp, large discontinuity at low x-ray energies (about 33 keV, at the "K-absorption-edge"). If an iodinated object were illuminated with a pair of x-rays whose energies straddled this K-edge, and one measured the intensities coming through the object, the (normalized) difference in these transmitted intensities would be a direct measure of the amount of iodine contained in the object (Figure 2). Macovski and colleagues filter the continuous x-ray spectrum into two narrow peaks in order to make these peaks simulate single-energy photons as closely as possible; the peak energies straddle the K-absorption edge.
The transmitted photons illuminate the radiographic film in alternating



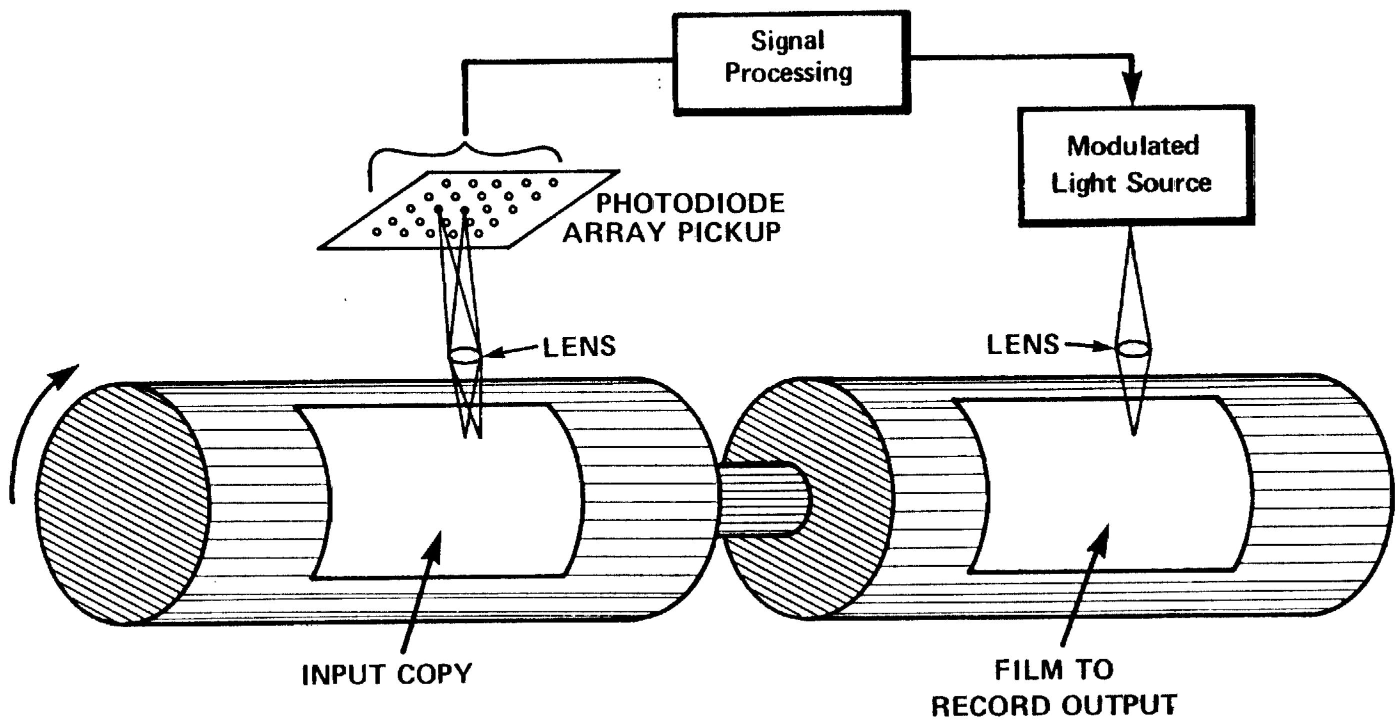
USE OF K-EDGE TO ENHANCE DETECTION OF IODINE

Figure 2

strips, so that the film is actually encoded with the difference information.

Such encoding can be done in either of two ways: First, two separate exposures are made as follows: A fine grating (0.5 mm spacing) made of lead-air-lead-air...etc. is laid atop the film cassette. For the first exposure, a filter which shapes the x-ray continuous spectrum into a bundle of photons peaking on the low-energy side of the K-edge is placed in front of the x-ray source, and an exposure is made. Then the lead-air-lead...etc. grating atop the film cassette is moved sideways (translated) by 1/2 period, so that the as-yet unexposed strips of film are available; a second source filter forming bundles peaking on the <u>high</u>-energy side of the K-edge is put in front of the source; and the second exposure is made. If done properly, the resulting image consists of alternating strips which differ only in the amount of iodine absorption; and to the naked eye, the image looks like a normal radiograph. The second method requires only a single exposure to make an image. A grating made up of alternating strips (again, 0.5 mm wide) of each type of peak-forming source filter is used. The illuminating x-rays passing through the object then possess these alternating-strip characteristics. (In this case, the lead-air-lead...etc. translating grating atop the cassette is not needed.) Both ways produce the same result: an image whose alternating strips have encoded information about the amount of iodine in the x-rayed object. Macovski then decodes these strips by pairs, using a decoding technique he developed for NASA (see <u>NASA Technology</u>).

A modification of this technique exploits the fact that bone and soft tissue



DECODING SCANNER

Figure 3

(equivalent to water) possess different absorptivities in the energy range below 100 keV. Therefore, if a combination of bone and soft tissue were to be illuminated with two monoenergetic x-ray beams, their intensities would be described by the following two simultaneous equations:

$$I_{\substack{low \\ rec'd}} = I_{\substack{low \\ incident}} \exp \left[\mu_{tissue}^{(low\ E)} \; Z_{tissue} + \mu_{bone}^{(low\ E)} \; Z_{bone} \right]$$

$$I_{\substack{high \\ rec'd}} = I_{\substack{high \\ incident}} \exp \left[\mu_{tissue}^{(high\ E)} \; Z_{tissue} + \mu_{bone}^{(high\ E)} \; Z_{bone} \right]$$

where all but Z_{tissue} and Z_{bone} (the lengths traversed) would be known, so that Z_t and Z_b could be solved for.

By using filters over the source which produce peaks in the 50 and the 80 keV region and by using the alternating-strip-exposure technique, an encoded radiograph can be produced. The resulting film is read out by a pair of photodiodes, analog-to-digitally converted for computer solution of both the thickness of bone and the thickness of tissue. The computer can be made to drive a light-source which, in synchrony with the reading diodes, can make a new film of either bone or tissue alone (Fig. 3).

A third technique, undergoing recent intensive development holds promise for making images of an iodine-containing coronary artery in 1-3 seconds. Although the movement of the artery will, of course, introduce some artifact, the image will be sharp and clear since each exposure is made in a few milliseconds. If successful, this technicue would be extremely useful in the diagnosis of stenosis or narrowing of the coronary artery.

Progress

The 115 keV clinical radiography machine is dedicated to this project; a hospital CT scanner in the Medical Center can be used briefly. Macovski's Stanford Medical Center laboratory is fully operational. Although some difficulty has been encountered with the construction of the alternating-strip gratings due to non-uniformity in some of the materials used, images can be produced by using the lead-air-lead...etc. grating atop the film, using two exposures as described previously. Work is continuing on improving the alternating-strip grating.

A theoretical study of the signal-to-noise ratio for various conditions (detectors, radiation doses, subject thicknesses, etc.) has been carried out. Experimental verification is now underway.

Using an existing CT scanner with two voltages and two auxiliary "peak-shaping" filters, experimental checks of S/N ratio have been made with various combinations of tissue-equivalent materials and iodine concentrations in simulated arteries; computer solutions to the simultaneous equations have also been obtained. From these investigations, a microcomputer is to be designed specifically for solving these equations. An experimental study has been also made of the radiation dose which would be given to the patient as a function of those intensities and energies chosen to give optimum S/N ratio.

Two papers have been written: 1) "Isolated Iodine Images Using Spatial-Frequency Encoding" by Macovski, Harrel, Strul, Yeh, and Chan (accepted by the Journal of Medical Physics to be published in the January-Februay, 1979 issue); 2) "Iodine Imaging Using Spectral Analysis" by

Macovski, a more complete description of the several lines of investigation, given at the Non-Invasive Conference at Stanford University in September 1978.

Plans

Emphasis is being given to preliminary work on the stenosis "snapshot" technique. Work to improve the alternating-strip gratings continues. Animal experiments have been made and additional ones are being planned. There has been strong commercial interest in this project, as described later in the Commercialization Section of this report.

PEDIATRIC ROENTGEN DENSITOMETRY

Objective

Fabricate and evaluate a roentgen densitometric system as a screening test for newborn infant cardiac shunts.

NASA Technology

The proposed system was first described by Dr. Louis Del Guercio and received the 1973 Gold Award from the American Academy of Pediatrics. The original system used an array of solid-state Gamma detector diodes developed for NASA by GE's Space Technology Products Division. Subsequent versions used lithium-drifted silicon diodes, while the most recent designs utilize Bismuth Germanate (BGO) crystal, optically coupled to "blue-enhanced" silicon photocells.

Background and Approach

The etiology of cyanosis in an infant is a problem routinely faced by the pediatrician and neonatologist. Cardiac involvement, superficially indicated (perhaps by heart murmur), must be confirmed to differentiate between an abnormal but functional flow pattern (not contributing to cyanosis) and a serious congenital cardiac dysfunction. The extant method of diagnosis for this problem is through cardiac catheterization. This procedure requires a skilled cardiologist, special-purpose facilities, is expensive and subjects the infant to some degree of risk. A pre-screening technique to evaluate the need for catheterization studies would be most valuable.

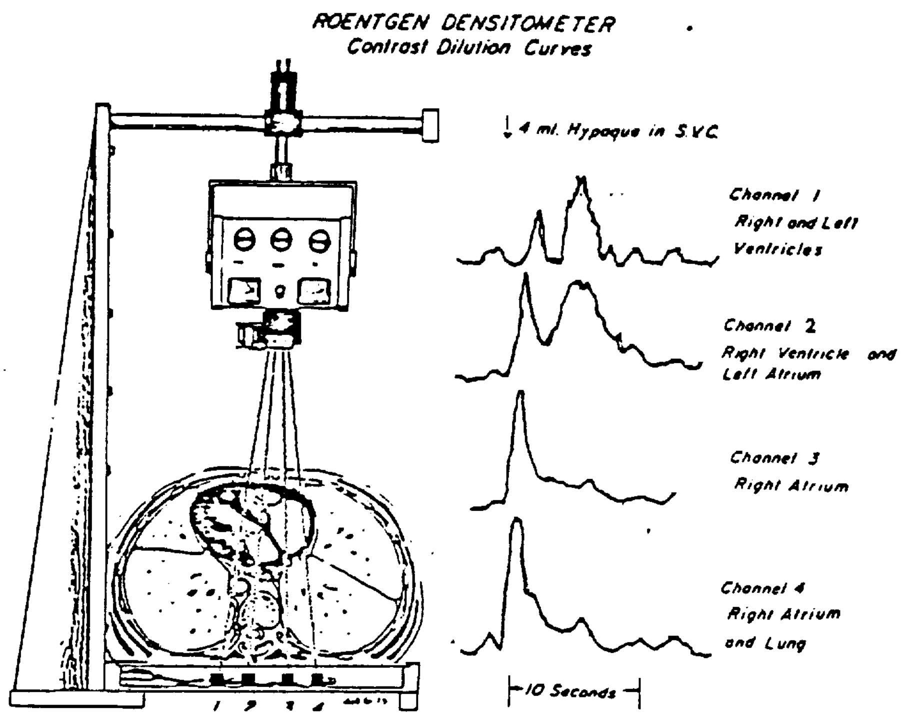


Figure 1: Roentgen densitometer configuration illustrating the recordings from four detectors receiving information from four x-ray beam trajectories piercing different portions of the cardiopulmonary anatomy.

A procedure for minimal risk screening of cyanotic infants to detect cardiac problems is being developed by Louis Del Guercio, M.D. of the New York Medical College.

This method involves a low-dose, nonradioactive, peripheral venous injection of a bolus of iodinated contrast material. This material, as it is passing through the heart chamber, intensity modulates x-rays directed through the heart, thereafter striking an array of six BGO-silicon detectors. The resulting detector signals are amplified and traced on a six-channel strip-chart recorder to yield a set of densitometric curves. A set-up of the instrumentation is illustrated in Figure 1.

The existance of intracardiac shunting, a primary cause of infantile cyanosis, can be ascertained by analyzing the morphology of the curves which reflect cardiopulmonic flow patterns. The curves can be categorized into four clinically significant groups corresponding to the occurence or non-occurence of shunting as follows:

1. Normal Circulation - bimodal curve with a rapid decay to baseline.
2. Left-to-right Shunt - bimodal curve with elevated inter-modal baseline and a prolonged decay.
3. Right-to-left Shunt - unimodal curve pattern with rapid return to baseline.
4. Bidirectional Shunt - unimodal curve with prolonged decay to baseline.

Examples of these curve types are shown in Figure 2.

The curves are further analyzed via a least mean square fit program using a Sonic Digitizer coupled to a Wang programmable calculator.

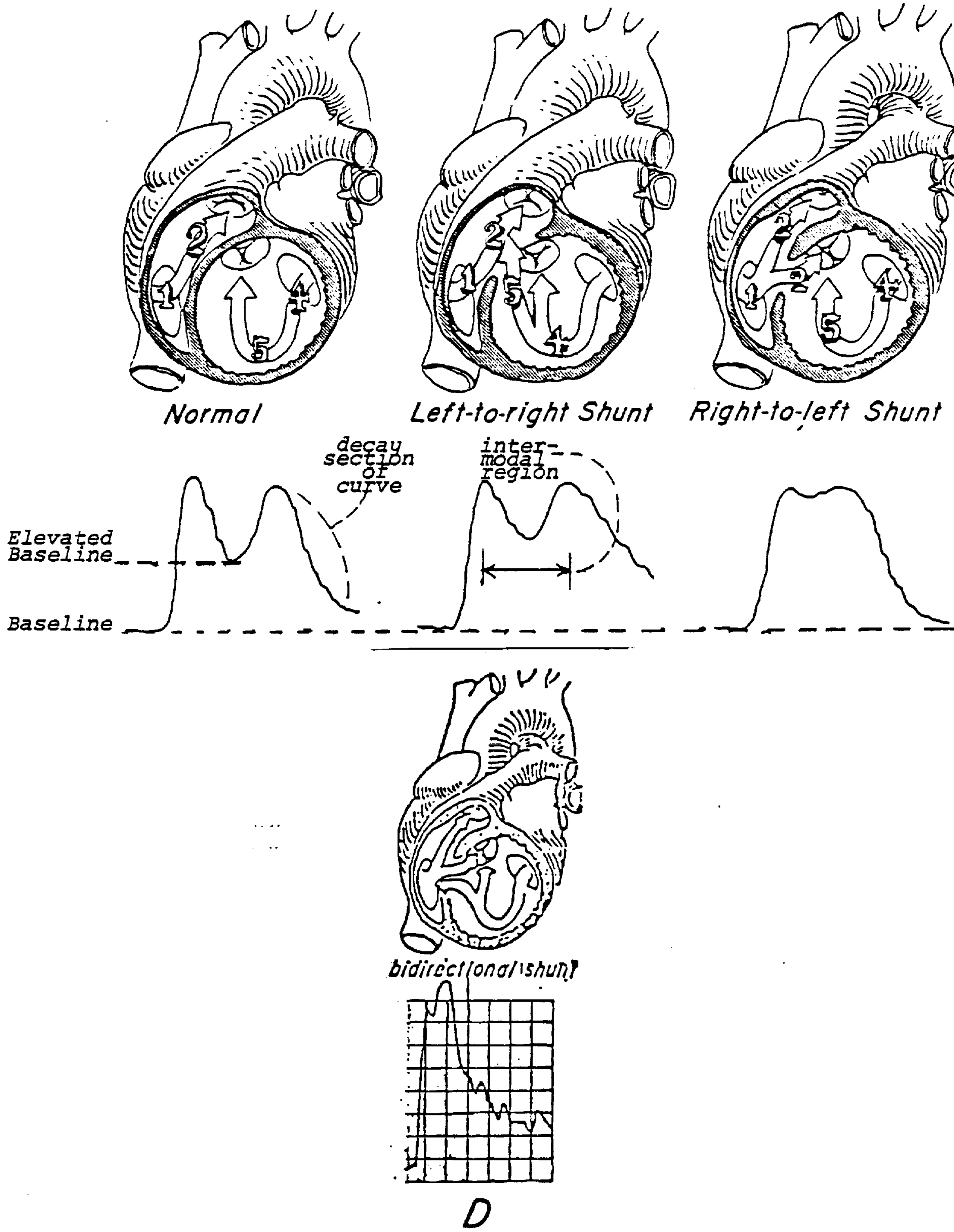


Figure 2: Examples of the four types of curve morphologies obtained withthe Roentgen Densitometry System

The values for the exponential decay constant and the time to first peak can be plotted as in Figure 3. Each curve morphology has a distinct two-dimensional region on the graph.

Progress

Recently, arrangements have been made to purchase three (3) BGO-silicon detector array systems with accompanying amplifier and signal conditioning electronics. Each system is comprised of six (6) detectors along with two spares.

Dr. Del Guercio and his colleagues are continuing to document curve morphologies associated with intracardiac shunting and other flow pattern abnormalities through dog studies. A clinical protocol is in preparation and will be distributed to the other proposed investigators.

Plans

The detector arrays should be ready for use in early April, 1979. A roentgen densitometry system will be sent to each of the following institutions:

1. Stanford University Medical Center - (P.I.s: William Brody and James French).
2. Columbia University, Div. of Pediatric Cardiology (Welton Gersony).
3. Harvard Medical School (Eugene Braunwald).

It is anticipated that the procedure will be in clinical use by mid-summer of 1979.

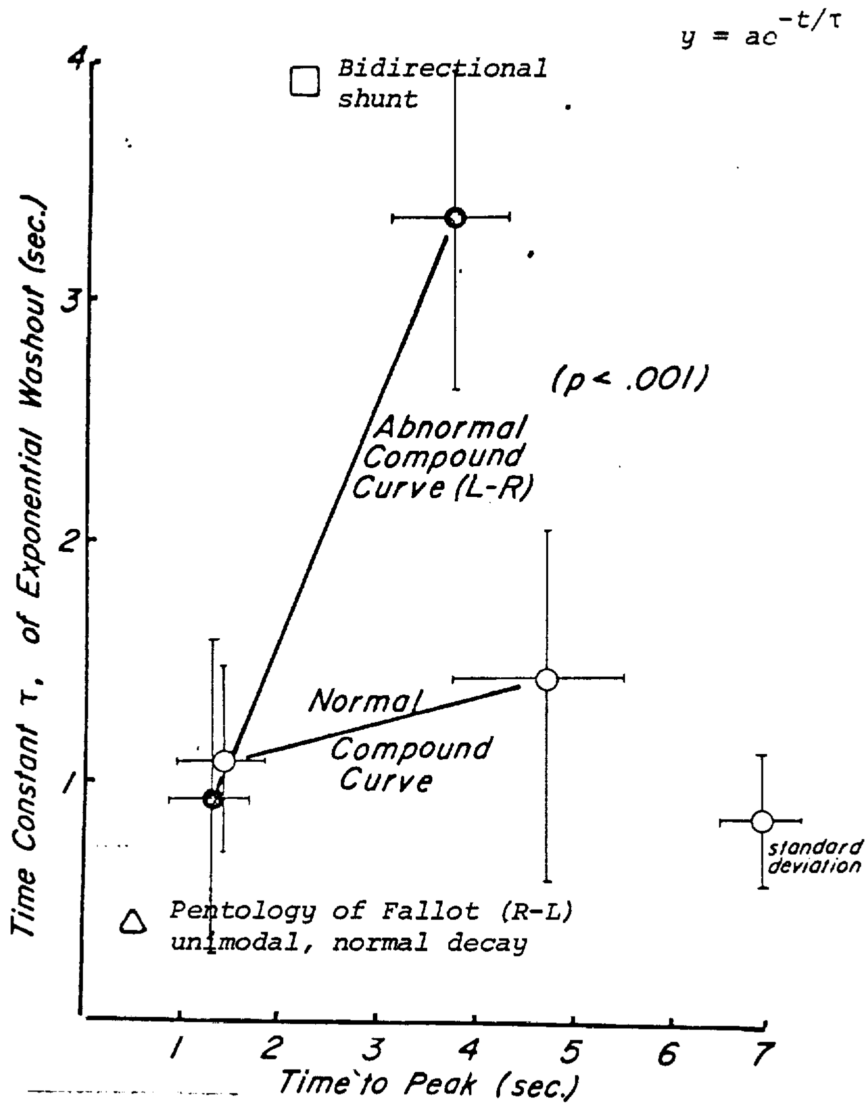


Figure 3: Plot of Exponential decay constant τ versus time to first peak. Note distinct regions associated with densitometric curve morphology.

WRISTCOM SYSTEM

Background

The WRISTCOM System - a tactile paging and communications system is being developed by the Digital Design Group of SRI International to meet the communications needs of deaf-blind clients of the Helen Keller National Center for the Deaf-Blind located in Sands Point, NY. The system enables the wearer to receive messages, time signals, or warning of a fire alarm and to send acknowledgement signals or even request aid from the Center's communications base.

Approach

The two principal components of the system are a base station and a small self-contained, on-body package worn on the user's wrist (See Fig. 1). This wrist unit incorporates a transmitter and receiver, a microprocessor-based controller, and two types of tactile stimulators.

The base station is able to address the users in three different ways: 1) simultaneously to all body units, as in the case of time signals or a fire alarm; 2) to a selected group such as only certain groups of patients or staff members; and 3) individually to each on-body unit for such messages as "You have a visitor" or "Please come to the lobby." The system operates in any one of seven distinct prioritized modes--two automatic polling modes where the individual wrist units are sequentially addressed and tested and five manual modes which permit the base station to send fire alarm, time, or individual messages to the wearers.

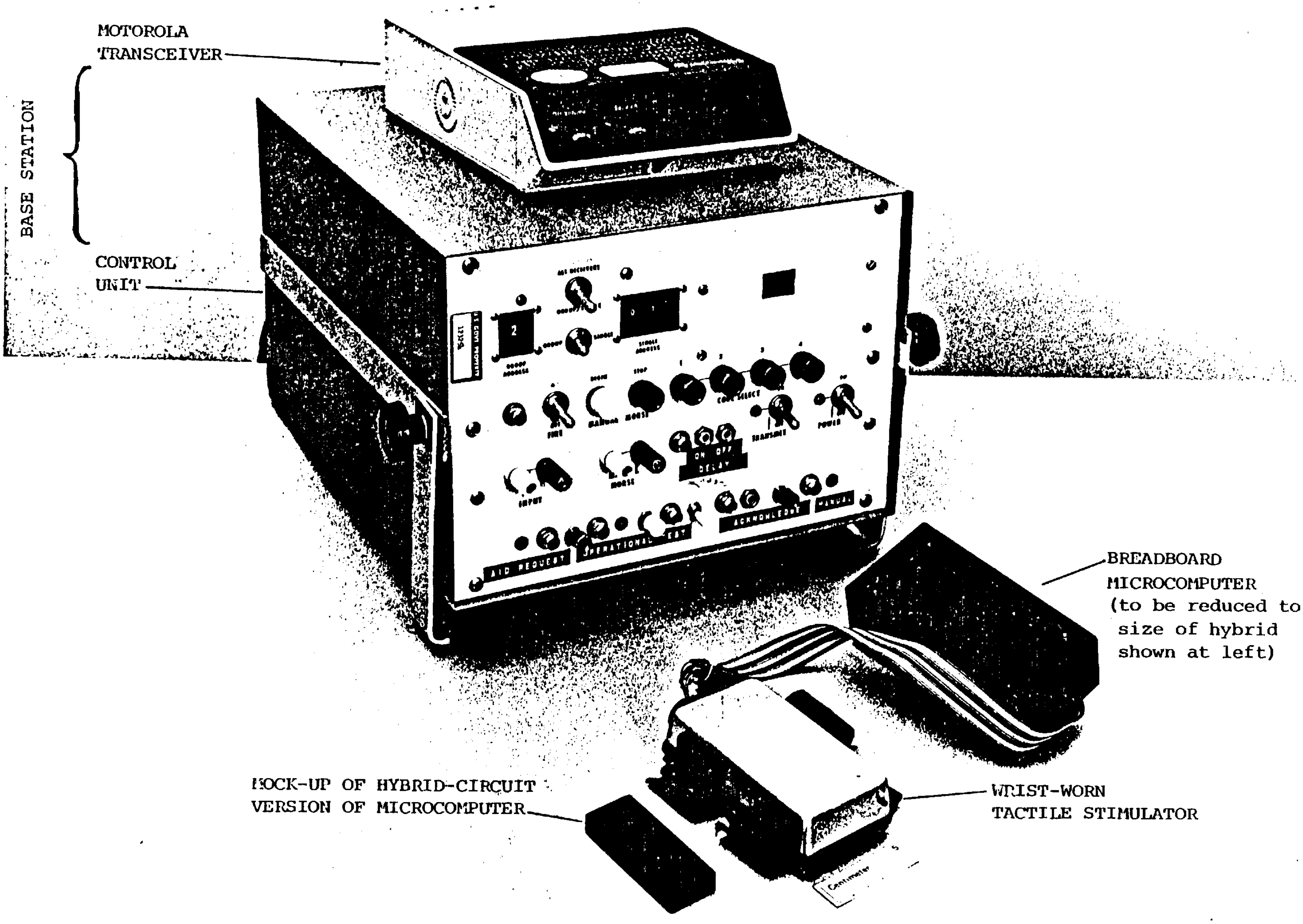


Figure 1: WRISTCOM SYSTEM - TACTILE COMMUNICATIONS DEVICE FOR THE DEAF-BLIND

The on-body units are automatically tested every half hour for operational integrity when the base station goes into an "OPTEST" mode. The balance of the time the system is searching for an "AID REQUEST" from any of the users. When a user-initiated aid request is detected, the operator at the communications base station canthen send a reassurance message back to the wearer to acknowledge receipt of the aid request and indicate that assistance is on the way. The system also allows users to acknowledge receipt of various messages encoded in Morse code characters.

To ensure data integrity and signal accuracy, signals sent to the wrist units are digitally encoded and repeated 5 times in less than one second. The wrist unit then processes the data string, checks it on an internal microcomputer, and generates a signal to drive the appropriate tactile stimulator.

Progress

During 1978 the operational breadboard was completed, tested, and demonstrated to representatives of the National Center of the Deaf-Blind and the Smith-Kettlewell Institute. The system was also displayed at the Interagency Conference on Rehabilitation Engineering in Washington, DC. Design of the wrist package and its associated internal electronics was also completed. An integrated circuit hybrid package containing the microprocessor and all of its associated electronics is being fabricated and will be completed by February 1979.

Plans

Within the next year an additional 12 wrist units and one additional base station will be built for in-use testing at both the National Center for the Deaf-Blind and the Smith-Kettlewell Institute.

The system's self-contained wrist package and its ability to transmit "aid request" signals make it applicable to other special environments such as nursing homes and senior citizen residences. These and other applications will be explored further pending completion of the first two evaluations.

EMG BIOTELEMETRY FOR PEDIATRICS

Objective

To apply aerospace biotelemetry expertise to the problem of monitoring the electromyogram (EMG) of children with gait abnormalities.

Approach and Progress

The EMG Gait Analysis Biotelemetry Project, begun in 1972, involves the transmission of EMG signals from opposing leg muscle groups to a computer-based data acquisition system. This EMG information is correlated with leg motion, indicated by foot switches, and enables the orthopedist to determine which muscle groups are contracting out of normal gait sequence.

The telemetry system designed by NASA engineers consists of six small, crystal-controlled RF transmitters. With attached electrodes, these transmitter packages are placed on opposing muscle groups (Figure 1). The 174-216 MHz transmission band is used for the required carriers. Each transmitter has a flat frequency response from 20-2000 Hz. The operating range is approximately 15 meters.

The EMG signals are displayed on an oscilloscope and a Honeywell 2106 Visicorder. A Data General Nova-2 minicomputer samples each transmitter channel at a 5 KHz sampling rate and stores the samples on disk memory (10 megabyte capacity). A patient's gait analyzed for 25 seconds, a typical run, requires 4.06 megabytes of storage.

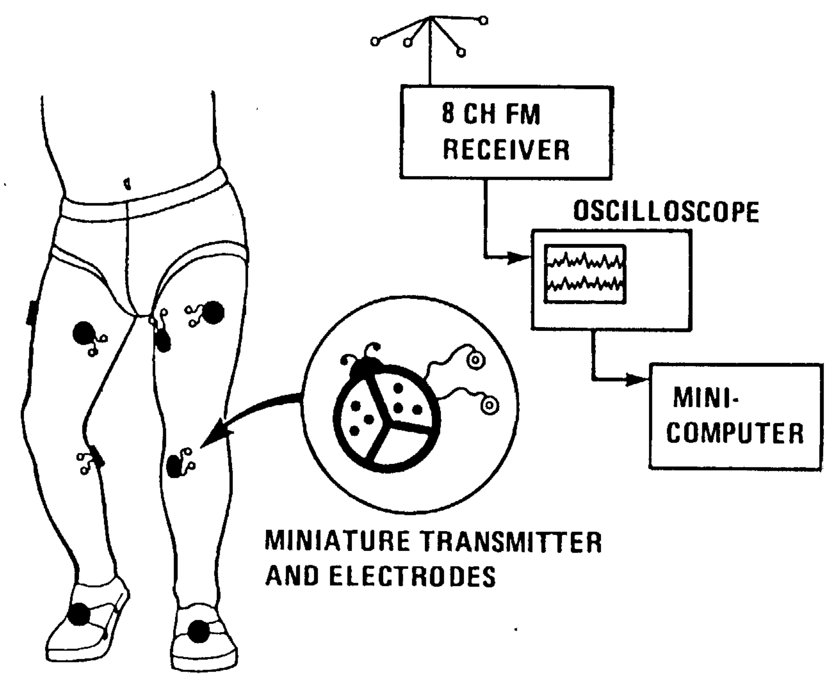


FIGURE 1 - Pediatric EMG Biotelemetry System

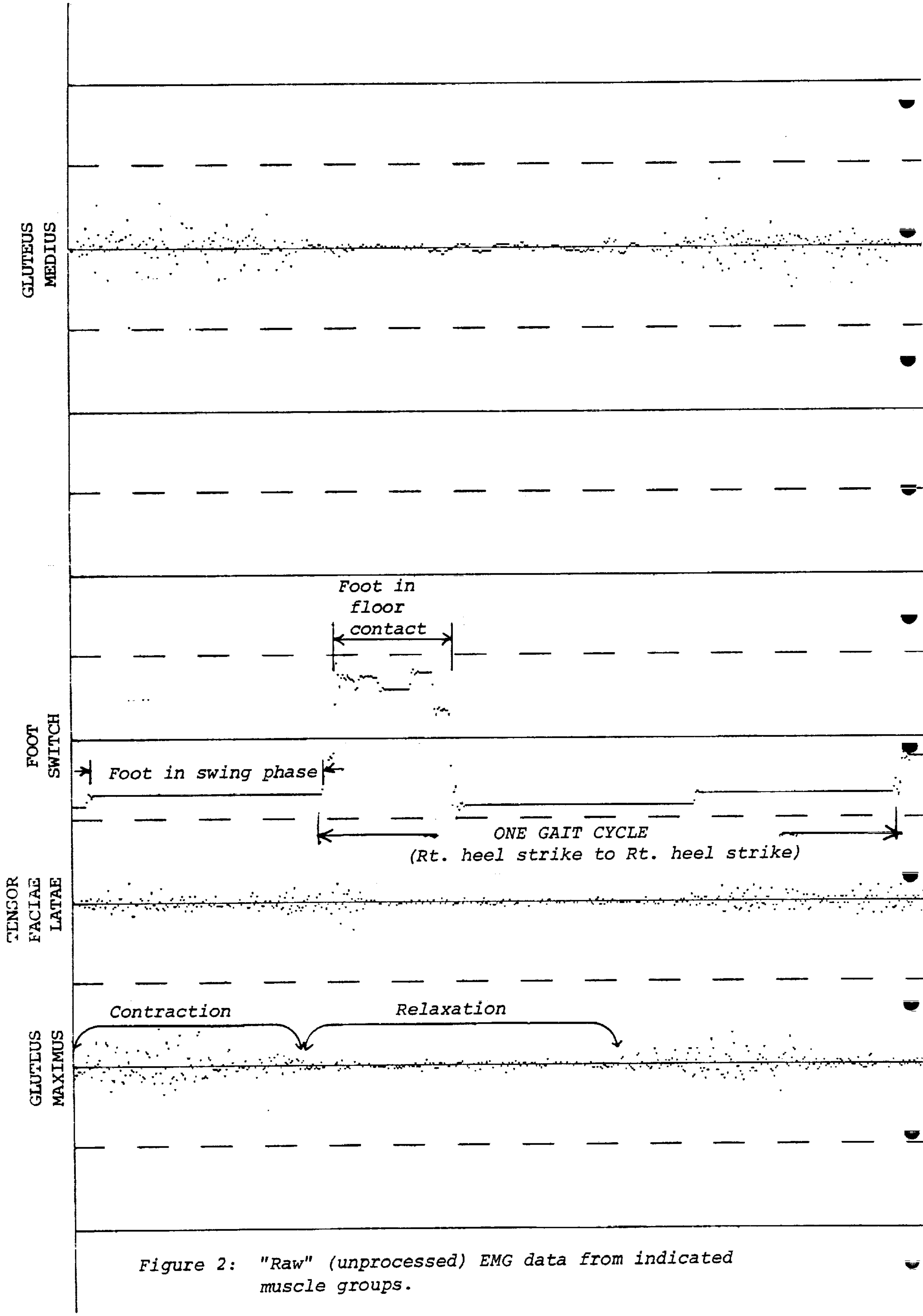


Figure 2: "Raw" (unprocessed) EMG data from indicated muscle groups.

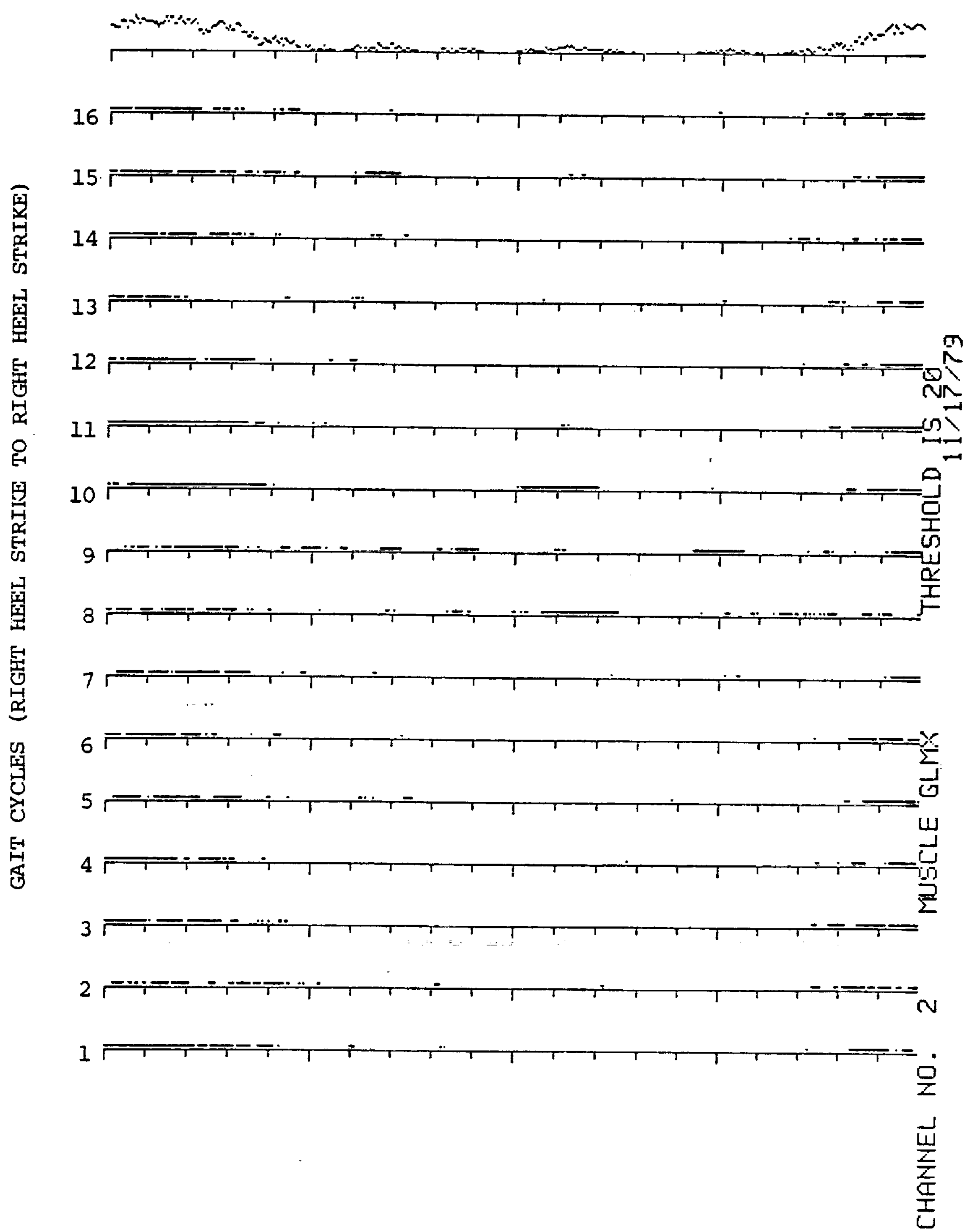
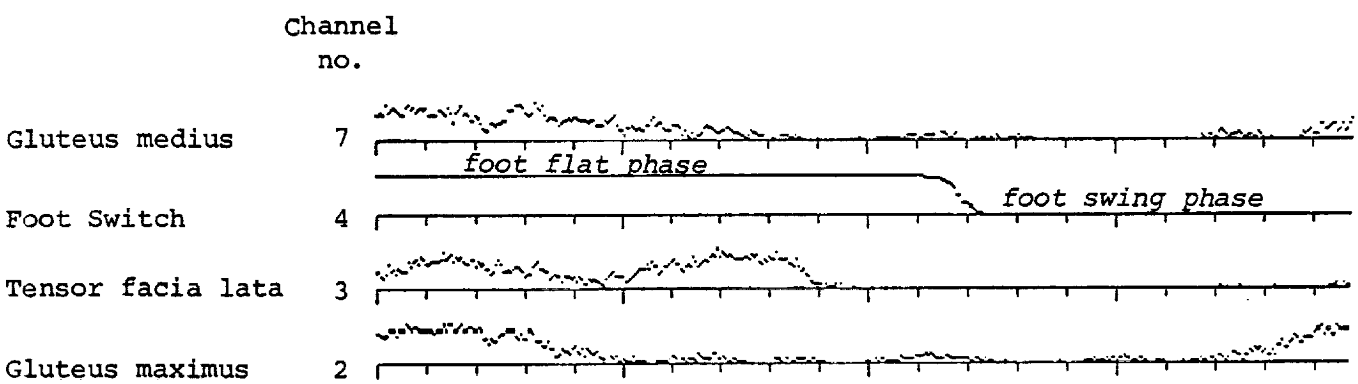


Figure 3: Rectified and averaged EMG data (top line) during 16 gait cycles. Solid lines indicate duration of right heel contact.



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CHANNEL NO.	2	MUSCLE	GLMX	THRESHOLD IS	20
CHANNEL NO.	3	MUSCLE	TFLT	THRESHOLD IS	20
CHANNEL NO.	4	MUSCLE	FOOT	THRESHOLD IS	0
CHANNEL NO.	7	MUSCLE	GMED	THRESHOLD IS	30

Figure 4: Summary of data for three muscle groups

The data processing and reduction involves the detection of the EMG envelopes. Editing software enables the user to eliminate artifacts. Results from a clinical "run" are presented in Figures 2 through 4. Clinical evaluations have shown this technique to be an invaluable tool in the diagnosis of abnormal gait patterns.

Plans

The clinical success of this approach has kindled the interest of several medical and rehabilitative centers. L&M Electronics (Daly City CA), the builder of the prototype biotelemetry system, has had several requests for information on this system.

The transmitters have had some problems associated with their discrete component fabrication. Signal drop-out and voltage artifacts have occurred from time to time. The combination of heightened medical interest for the gait biotelemetry system, along with the annoying problems due to its discrete component construction, warrants consideration of incorporating the transmitter design into a hybrid package.

DETERMINATION OF BONE PROPERTIES BY MECHANICAL IMPEDANCE

Objective

To assist in the clinical evaluation of a non-invasive, mechanical impedance technique for measuring bone strength.

Background

Scientists at the NASA-Ames Research Center have conducted extensive research on the potential deleterious effects on bone density produced by the zero gravity of space flight. Skylab astronauts, during their 84-day voyage, experienced loss of bone calcium and increased excretion of calcium in the urine. These effects are similar to those seen in the elderly and in patients confined to bed for long periods of time. NASA scientists and university engineers have collaborated on the development of a mechanical device to measure the driving point impedance of bone. This work has led to the following publications on the theoretical analysis of bone integrity as well as research applications in man and monkeys:

1. Thompson, G.A.; Young, D.R. & Orne, D.; In Vivo Determination of Mechanical Properties of the Human Ulna by Means of Mechanical Impedance Test: Experimental Results and Improved Mathematical Model; Medical and Biological Engineering; May, L976 pp. 253-262

2. Orne, D. & Young, D.R.; The Effects of Variable Mass and Geometry Pretwist, Shear Deformation, and Rotary Inertia on the Resonant Frequencies of Intact Long Bones: A Finite Element Model Analysis; J. Biomechanics; vol. 9, pp. 763-770, 1976

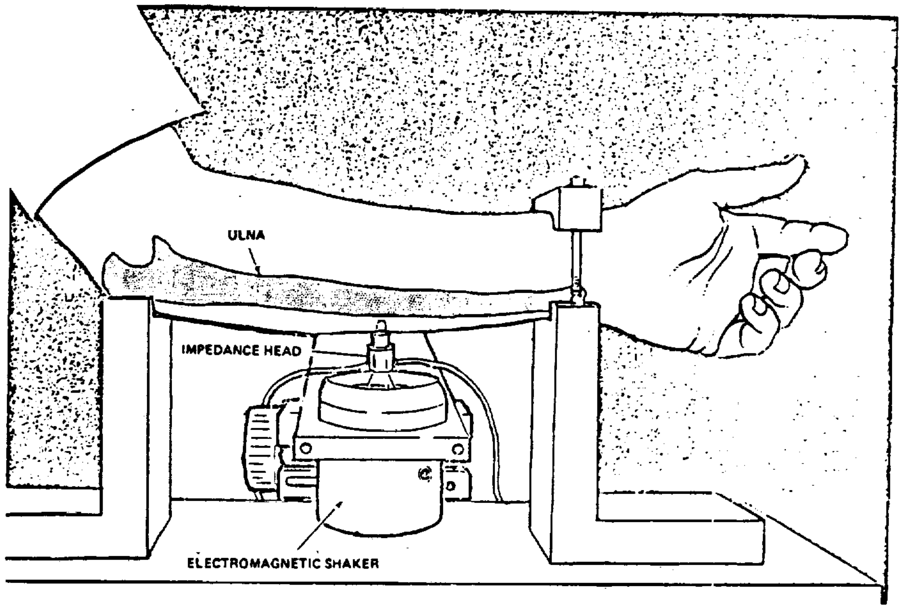


FIG. 1 ARM SUPPORTS AND DRIVING SYSTEM [Thompson, 1973a]

Table 1 - Subjects With Injury to One Arm

Subject	Uninjured	Injured	Comments
1	13.7	11.4	Wrist fracture, 1 yr. ago
2	15.7	5.1	Midshaft ulna fracture, 1 mo. ago
3	12	8.8	Hand fracture
4	11	12.0	Wrist fracture
5	12.3	8.9	Wrist fracture
6	15.8	14.3	Shoulder and arm fracture, 2X
7	13.5	14.8	Hand fracture, 3 mos. ago
8	14.5	6.1	Severe fracture, ulna, 2 yrs. ago
9	14.7	5.7	Fused wrist - no grip, no use 4 yrs.
10	12.8	8.2	Injured shoulder, 50% use for 3 yrs.

3. Young, D.R.; Howard, W.H. & Orne, D.: In Vivo Bone Strain Telemetry in MOnkeys (m. Nemestrina); J. Biomechanical Engineering; vol 99, May, 1977

Approach

The method used measures the bending rigidity of bone in vivo by recording its response to harmonic oscillations and determining mechanical impedance at the driving point. The apparatus used employs an electromagnetic shaker driven by an auto-oscillator and amplifier which produces low-distortion harmonic signals at a frequency of 40 Hz. An impedance head containing piezoelectric crystal transducers allows measurement of both force and acceleration. To perform the impedance measurements on the ulna, the subject's arm is placed in supports as shown in Figure 1. The vibrations are transmitted to the ulna at a point approximately 60% of the distance from the elbow to the wrist. The driving probe itself has been reduced in size in order to minimize the inherently non-linear effects of the skin and soft tissue overlying bone. The signal corresponding to acceleration is electronically integrated to obtain displacement. The analog recording of force and displacement allows calculation of driving point impedance. The driving point impedance is then used to calculate bending rigidity and axial buckling load, the load or weight the bone can support without fracturing.

Progress

An automated control system using a microprocessor has been developed by Oxbridge, Inc. in cooperation with Dr. Charles Steele, Stanford University Department of Engineering. This microprocessor-based system permits recording of force and displacement very rapidly. In addition, data from a number of tests can be accumulated and averaged in a few seconds. The force and displacement signals are converted to digital form (50 points per half cycle) and averaged over 8 cycles to eliminate fluctuations due to subject motion. The test is repeated at 5 levels of static loading, controlled by an axial servomotor and load cell. The consistency of the results for bone stiffness at different static loads serves as a check of reliability. The entire procedure, including print-out of results, requires about 10 seconds with the automated microprocessor system.

Progress

Early in the year tests using the bone stiffness analyzer were conducted at the Stanford University Orthopedic Clinic. The correlation between measured values of ulnar stiffness and a subjective measurement of bone strength were excellent. The calculated axial buckling stiffness is very high in physically active individuals, such as water skiers and weight lifters. Patients who have had an injury to one arm which has resulted in disuse had axial buckling indices one-third those of the opposite, uninjured arm. Data on 10 subjects is shown in Table 1. These preliminary clinical tests have shown that the axial buckling index, measured with the automated bone stiffness analyzer, is a good indicator of bone mineral content and strength. Furthermore, the test is simple, fast, inexpensive, completely painless, and safe for the subject or operator.

Based on these promising early clinical results, the Biomedical Applications Team has assisted in preparing a proposal to NASA Technology Utilization for further hardware refinement and additional validation. The proposal, however, was not funded.

In order to obtain additional clinical results and, in particular, serial studies to look for slowly evolving changes, the bone testing instrument was then used on a small series of patients at the Palo Alto VA Hospital who were undergoing dialysis for kidney failure. These patients frequently develop a form of bone thinning referred to as renal osteodystrophy. However, because of their age, difficulty cooperating due to their disease, and difficulty positioning their arms on the bone tester due to their arteriovenous shunts, this attempt was discontinued.

Plans

In January, 1979 a study will begin at Stanford University entitled "Effects of Acute and Habitual Exercise on Plasma Lipoproteins." This is a 3-year program funded by the National Heart, Lung and Blood Institute. Its purpose is to look at the effects of exercise on blood chemistries, in particular, levels of high-density lipoprotein and low-density lipoprotein. A group of 65 initially sedentary men between the ages of 30-55 will be placed on a supervised progressive physical conditioning program. A group of 35 men will remain sedentary and serve as the control group. These two groups, each undergoing a different level of physical activity and being tested at 3-month intervals, would provide an excellent group for a longitudinal study of bone strength measurements using the mechanical impedance bone tester.

Current plans are to move the bone tester from the Palo Alto VA Hospital to the Cardiac Rehabilitative Center at Stanford University Medical Center in January. The measurements of bone strength will be performed by a graduate student in Mechanical Engineering. The results of these tests will be made available to the Lipid Research Clinic Study Group and correlated with other measurements related to physical fitness and cardiovascular conditioning. The present bone testing instrument requires that the bone be placed in a horizontal position on top of the impedance head. Previous experience and mechanical engineering analysis indicate that better measurements could be made if the bone were in the vertical position with the impedance head providing horizontal displacements. This new configuration would also permit testing of the tibia (shin bone) which would be desirable in future orthopedic as well as physical fitness studies. In the spring of 1979 a proposal will be submitted to NASA to make these hardware modifications. Co-funding from other government agencies and the medical device industry will be sought. In addition, a representative of Syntex, a pharmaceutical company which has recently marketed a new anti-arthritic compound, will investigate potential applications of this instrument in arthritis research in February, 1979.

CARDIOVASCULAR MAGNETIC MESUREMENTS

Objectives

To apply NASA technology in the fields of superconducting magnetometry and adaptive filtering to the recording of more accurate magnetocardiograms and cardiac blood flow signals.

Background

Recent developments in superconducting quantum interference detectors (SQUIDs) have made it possible to measure the very weak magnetic fields emanating from the cardiovascular system in man. These magnetic measurements can be made without making body contact. Although further study of the magnetocardiogram (MCG) is needed to verify its clinical potential, it is clear at present that the MCG is due to electric currents within the heart producing a magnetic dipole which can be accurately recorded because of the spherical anatomical orientation of surrounding intrathoracic tissues. Cardiologists and physicists at Stanford University Medical School have recently reported in Science (vol. 198, pp. 1159-1162) that recordings made in patients with bundle branch block (an abnormality of the conductive pathways running through the intraventricular septum) have shown marked differences between their ECG and the MCG (Figure 1). These clinical results are in agreement with mathematical theory which shows that the ECG is more sensitive to the radial component of currents, while the MCG is more sensitive to the tangential components. These clinical results indicate that the MCG has potential for complementing the ECG in making cardiac diagnoses.

Researchers study heart's magnetic field

Stanford researchers have found that the measurement of the magnetic fields of the heart provides information about the conduction of impulses not reflected in conventional electrocardiography.

The technique may increase reliability in the diagnosis of heart disease.

Results of initial clinical studies using a SQUID differential magnetometer were reported in the Dec. 16 issue of *Science* magazine by Drs. William Barry, William Fairbank, Donald Harrison, and their associates.

The device measures magnetic fields produced by the flow of charged particles, called ions, through heart muscle cells. Ionic flow, which occurs during muscle contraction, also generates the electric fields measured in the electrocardiogram (EKG).

The differential magnetometer cancels out exterior magnetic fields which otherwise would interfere with the reading of the heart fields.

SQUID stands for superconducting quantum interference device. It amplifies the cardiac magnetic signals so they can be measured. The signals are processed and displayed in graphic form similar to the EKG.

According to Dr. Harrison, head of the division of cardiology and holder of the endowed William G. Irwin Professorship of cardiology, the EKG cannot diagnose certain heart conditions which involve abnormal electrical conduction through the heart.

Harrison conducts clinical testing of the device with Drs. Richard Meltzer and Jerry Griffin.

"Magnetocardiography may be helpful in diagnosing potential heart attacks which result from these conduction abnormalities," says Harrison. "It will complement but not replace the EKG.

"Many of the cellular properties related to the spread of impulses in the heart are not understood," he says. "The magnetocardiogram (MCG) will provide new insight into these properties."

The magnetic fields produced by the heart are very difficult to measure because they are one million times weaker than the earth's magnetic field, says Mark Leifer, graduate student in applied physics.

Leifer directs the development of magnetometry techniques with Prof. William Fairbank in the Department of Physics.

Previous efforts to pick up the tiny cardiac fields were hampered by magnetic interference, including power-line noise and even magnetic noise from cars driving along the street outside.

At Stanford this background noise was eliminated by placing the patient at the bottom of a 25-foot well lined with magnetic shielding.

The new SQUID magnetometer allows measurement at ground level without magnetic shielding, says Leifer.

Mark Leifer, graduate student in applied physics, adjusts the SQUID differential magnometer in a mock treatment set-up.

Figure 1.

Stanford University Medical Center
News Bureau Release - February 16, 1978

These recordings have been made at the bottom of a pit, 25 feet in depth, lined with molypermalloy magnetic shielding to reduce both the static magnetic field of the earth and the magnetic noise associated with the typical laboratory environment.

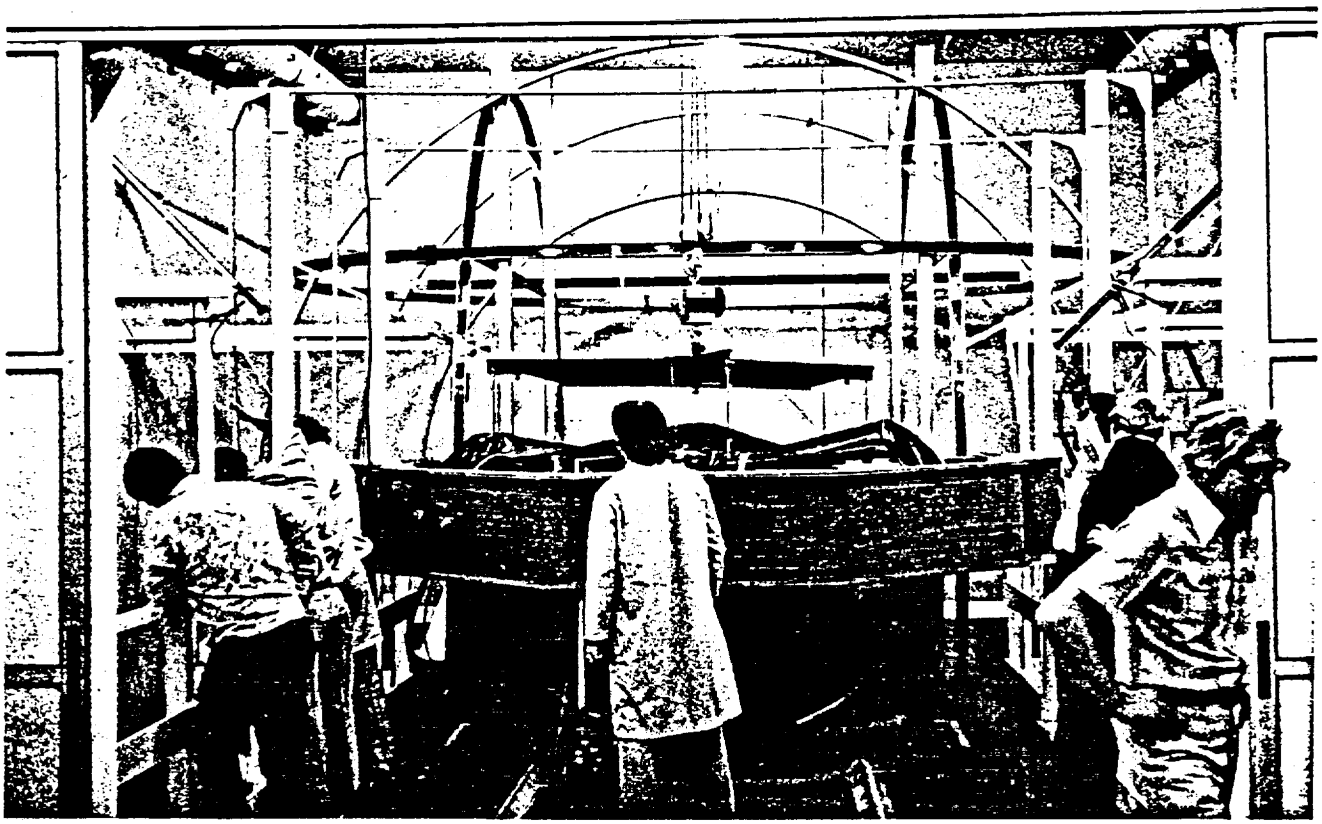
These investigators have requested NASA assistance in developing a much smaller, mobile, magnetic shielding device which will permit recordings of MCG within the hospital setting. They are also interested in measuring the magnetic signals associated with cardiac and thoracic blood flow.

NASA Technology

Over the past 10 years the NASA-Ames Research Center has been a leader in the development of magnetic field detection technology. Contracts resulting from NASA research in cryogenics and superconductivity have led to the commercial development of SQUID systems. The NASA-Ames Research Center has a unique Magnetics Test Facility which houses helium-cooled Dewar systems, large Helmholtz coil systems, and extensive cryogenic instrumentation developed for satellite projects, including the Pioneer Venus Probe and the Infrared Astronomical Satellite. The need to measure very weak magnetic fields from orbiting satellites and to render the satellite itself magnetically "clean" have further advanced the SQUID gradiometer technology.

Ernest Iufer, manager of the NASA-Ames Magnetic Test Facility, is interested in working with Stanford cardiologists and physicists in designing and building a coil system for unwanted magnetic interference and producing a sufficiently strong, uniform and stable magnetic field for conducting cardiac output measurements. He has proposed that existing orthogonal coil sets, used for creating large uniform magnetic fields

Figure 2.



A78-0072-20

Fifty Gauss demagnetization of Pioneer Venus Orbiter Spacecraft underway within the Non-Magnetic Building at NASA-Ames Research Center. Twenty-foot diameter, three-axis Helmholtz coils in the background.

(NASA photo courtesy of Ernest Iufer.)

for spacecraft testing, be used to demonstrate proof of concept prior to fabricating a smaller portable coil set for use in the hospital (Figure 2). Although stability requirements for making blood flow measurements exceed the current state-of-the-art in industry, coil systems already developed by Ames for research in earthquake forcasting have achieved angular stability of better than 5 parts per million, which is more than adequate for this medical application.

Approach

NASA engineers would work with physicists and cardiologists from Stanford University and Vanderbilt University to design an portable coil system which would provide the necessary magnetic shielding for high-fidelity MCG recordings as well as the 30-50 gauss uniform field for blood flow measurements. Design concepts would be tested using existing coil system and support equipment available at Ames. Advanced "adaptive filtering" techniques also developed by NASA-Ames for earthquake forecasting research would be incorporated to further improve the signal-to-noise ratio. The coil system would be fabricated at Ames and coupled to a second-derivative SQUID gradiometer to be loaned from Vanderbilt University. Liquid helium and necessary computer facilities are available at both Stanford and Ames. A $230,000 grant proposal has been submitted to the N.I.H entitled "Clinical Applications of Magnetometry in Heart Disease" and would facilitate clinical evaluations with the NASA magnetic coil system.

Progress

The proposal to NASA entitled "Cardiovascular Magnetic Measurements" has been approved and the preliminary engineering calculations, in collaboration with the Stanford physicists and cardiologists, have begun. Initially, standard Helmholtz coil systems will be evaluated for cancelling the earch's magnetic field and providing the high intensity, 50 gauss field for blood flow measurements. Also being considered are designs which will use a superconducting coil in association with a SQUID differential magnetometer (see Figure 1) to permit even better recordings of both the MCG and blood flow. The Stanford University Division of Cardiology has designated the required clinical space for a Cardiovascular Magnetics Diagnostic Laboratory. The N.I.H. grant proposal has been approved and funding of clinical personnel will commence in February, 1979. Final specification for a dedicated magnetometer which could measure cardiovascular and neurological signals is in progress and a unit will be procured in the first quarter of 1979.

ICU SYNTHESIZED SPEECH ALARM SYSTEM

Objective

To transfer NASA expertise in aeronautical communications technology to the problem of critical communications in the Intensive Care Unit (ICU) environment.

Background

Every major hospital contains one or more intensive care units for intensive monitoring and care of the critically ill patient. Survival of these patients depends upon careful monitoring of vital signs and immediate response by the nursing staff. The vital signs most frequently continuously monitored are the electrocardiogram, blood pressure, and respirations. When these vital signs exceed certain preset values, an alarm consisting of an audible tone or small light is activated.

A fairly common situation exists at the Martinez V.A. Hospital in Northern California which has its coronary care, respiratory, and surgical ICU's housed in a large, open, 16-bed ward. Physiological signals are displayed both at the bedside and at a central nursing station. In practice the audible tone and warning light have the following limitations:

a) It is not possible for the nursing staff to continuously watch for the warning light on the monitor while performing their many other nursing duties.

b) The high ambient noise level, due to such equipment as respirators, suctioning devices, telephones, television, and traffic, increases the liklihood of delay in response to a simple audible tone alarm.

c) The existing warning devices do not indicate the nature of the problem and require that the nurse go over to the monitor to see which alarm was sounded and which patient is in distress. This naturally leads to a less than optimal response-time to emergency situations.

In summary, existing warning systems do not seem to provide optimal communications to the nursing staff in a large, busy, and noisy intensive care unit setting.

NASA Technology

This problem provides an opportunity for a straight-forward application of communications systems technology, using synthesized speech, which has been under investigation for a number of years at the NASA-Ames Research Center. Experimental systems have been developed to provide synthesized voice output of aircraft altitude, air speed, sink rate, deviations from intended flight path, and other time-critical parameters. The expertise in programming speech synthesizers to provide intelligible and appropriate verbal messages to warn pilots of critical malfunctions is directly applicable to this problem of alerting the nursing staff to critical changes in the medical status of patients.

Approach

NASA-Ames Research Center technologists propose to use synthesized speech warning messages to alert the nursing staff to both the nature of the problem (i.e. respiratory arrest, sudden decrease in blood pressure, cardiac arrest, significant changes in heart rate, etc.) and the location (bed number) of the patient in distress.

The Martinez ICU is already equipped with bedside monitors which can be set to trigger an alarm when certain preset thresholds are exceeded.

NASA scientists have suggested that the voltage signals from these monitors be converted to drive a microprocessor and that the microprocessor be programmed to translate these voltage levels into instructions to drive a speech synthesizer. With programs to drive the speech synthesizer supplied by NASA scientists, it is expected that highly intelligible speech will be produced. The synthesized speech output will be amplified and broadcast over speakers placed at appropriate locations throughout the ICU.

Progress

Members of the Biomedical Applications Team and NASA-Ames scientists visited the Martinez V.A. Hospital to determine the general requirements of the ICU and to observe directly the constraints and difficulties presently encountered in its present set-up. The meeting included representatives of the V.A. engineering and surgical staff who indicated that the existing monitoring instrumentation, as well as an IMSAI-8080 microprocessor system, with seven-channel analog to digital converter, would be available for use in a synthesized speech warning system. Although the hospital has a very capable engineering staff, they have no previous experience with eliciting user-design preferences for message warning, speech synthesizer programming, and evaluating synthesized speech alarm systems.

After a return visit by the Martinez staff to both Ames and Stanford, it was decided to proceed with a formal proposal to NASA to cover the cost of hardware and technical support directly related to the synthesized speech portion of the system. The bedside monitors, central nursing station displays, microprocessor, and A to D converter have already been provided by the V.A. In addition, a proposal will be submitted to the V.A. to cover the personnel costs involved in planning, maintaining, and evaluating the system.

Work has begun in eliciting nursing staff preferences for the warning messages to be used. A questionnaire, designed to elicit the user preference, was patterned after one developed by Dr. Simpson at Ames for cockpit warning messages.

Plans

The proposal to NASA has been funded and the project will begin as soon as an interagency transfer of funds from NASA to the VA Hospital in Martinez is completed in early 1979.

COMMERCIALIZATION ACTIVITIES

COMMERCIALIZATION ACTIVITIES

One of the technology transfer process endpoints is the commercial transfer of new technology. Each of the instruments discussed in the Technology Transfer Projects Section has commercialization potential. This section highlights projects which have made substantial progress toward being accepted by the medical industry.

The commercialization process begins by determining if instrumentation is currently commercially available which serves the same function as the proposed new technology. Next, a survey of physicians, engineers, and medical device manufacturers is conducted to determine the need and desirability of a new approach. Such determinations are made through market surveys, conducted by the IIT Research Institute (Chicago, IL), which is under contract to the NASA Technology Utilization Program.

A market survey for certain projects can be conducted based on the new concept alone. However, in most cases it is necessary to build a prototype and conduct preliminary laboratory and clinical tests to confirm the technical and medical feasibility of the new approach.

Brief commercial activity summaries for selected BATeam projects follow. Where applicable, each summary includes the following information:

1. NASA Patent Status
2. NASA Licensing Information
3. Market Potential
4. Potential Manufacturers - Interaction
5. Commercialization Strategy

Intracranial Pressure Monitoring

The intracranial pressure monitoring units presently being used in clinical trials at Stanford University Medical Center were fabricated by Konigsberg Systems, Inc., Pasadena CA, and are based on a NASA design. The most stable of these units have been used in chronic animal studies and short-term patient monitoring. The Konigsberg units were suitable for research applications and provided proof that the technical approach was sound. However, further research and development is required before the system is ready for routine use. Competitive proposals to further develop the ICPM into a commercial product were reviewed by the Biomedical Team in January, 1978. Pacesetter Systems, Inc., Sylmar CA, was selected on the basis of:

1. Best understanding of technical problems and suggestions for performance improvements;
2. Expertise in the areas of inductive powering, hermetic sealing, and quality control of manufacturing processes;
3. Adequate resources and experience in large scale manufacturing and marketing.

In March, the Biomedical Team signed a contract with PSI specifying delivery of 12 second-generation ICP transmitters, mounting hardware, and two energizer/receiver units. These units were scheduled for delivery in December, 1978. In May, the first design review was held at Stanford attended by representatives of the NASA-Ames Research Center, Stanford University Medical School, and top management and engineering personnel from PSI. The transmitter circuit design, mounting fixture design, and data from experiments on the titanium diaphragm were reviewed. Subsequently, Pacesetter's chief of R&D returned to Stanford to observe all phases of the surgical implant procedure and postoperative monitoring. A second design review was held in October at which time Pacesetter presented a working model of the mounting assembly and insertion tool. They proposed a major revision in the transmitter design to incorporate electronic auto-calibration which would require the use of hybrid circuitry, including an LSI chip and programmable read-only memory. Although it was anticipated that these changes will delay the delivery date at least 6-8 months, the consensus was that the suggested improvements were essential to the overall goal of a reliable, economical instrument which would be suitable for widespread use by nonengineering-oriented medical personnel. PSI is now preparing a revised production schedule following critical path methodology, with tasks performed in parallel where possible. The rate-limiting step is the scheduling of the hybrid circuits which must be subcontracted to an LSI manufacturer.

Nanophor

After several uneventful attempts to license this instrument to major U.S. firms (Arco Medical and Beckman Instruments), an exclusive license is to be issued in late February, 1979 by the NASA-Ames Patent Office to Satoris, Inc. Satoris is a large European-based firm which has acquired a U.S. manufacturing company (Plastics Technology, Menlo Park, CA) to produce and market the Nanophor.

Plastics Technology is planning the first production run of 200 instruments which will retail in the $5,000-6,000 range.

Four prototype devices will be delivered to NASA-Ames Research Center in early 1979. Two of these instruments will go to the Stanford University

Medical School for clinical evaluations. In addition, a detailed Operating Manual for the Nanophor has been completed by Dr. Grunbaum in association with the Stanford BATeam and the Ames T.U. Office. Printing of a specified number of the manuals will be available through NASA-Ames.

Pediatric Roentgen Densitometry

This procedure is not a stand-alone diagnostic tool but rather a screening technique to more appropriately select patients for cardiac catheterization. U.S. Patent 3,622,872 has been issued to Dr. Louis R. M. Del Guercio. The procedure has not, as yet, been licensed. The market potential has been estimated to be $16,000,000 (2,000 units @ $8,000/unit) according to an IIT Research Institute market survey. Of these 2,000 units, approximately 500 may find use in specialized pediatric centers and the rest would be used in smaller referring hospitals. Commercialization of the device will depend chiefly on its perceived value at the institutions performing the initial evaluation planned in 1979.

Versatile Portable Speech Prosthesis

Although there are communicative aids which produce visual and/or printed output, speech provides faster and more efficient communication for group and classroom participation and telephone conversation. Currently, there are a number of commercial devices which offer some speech capability, but each has one or more of the following problems:

1. Vocabulary is limited to prestored words and phrases.
2. Currently, only one device incorporates synthesized speech, with its inherent advantage - requiring less memory for

message storage. However, this device does not use syntax-variable intonation or contextual phonetic rules, which would give the speech greater intelligibility.

3. Programmable commercial devices require extensive training in order for the user to achieve intelligible speech. Even then, the programmed vocabulary cannot be stored.
4. Vocabularies are stored in programmable read-only memories, which are neither easily nor economically changed.
5. Most devices require use of a keyboard, excluding use by speech-handicapped individuals with severe motor coordination problems.
6. The keyboard and touch panel layout of vocabulary items inhibits rapid message construction. This is because language structure was not considered in the design.

One communications device requires that the user learn 1,000 three-digit codes. Using such a device would be cumbersome even for a person with normal motor function.

Commercial interest in the VPSP is very keen. Some current proposals are:

1. Votrax (a division of Federal Screw Works), which has donated two ML-1 speech synthesizing units (approx. $40K) to the project, is very much interested in manufacturing and marketing possibilities of the VPSP.
2. Telesensory Systems, Inc. is interested in exploring the possibilities of mating the VPSP with their Aurocom units, thus replacing the CRT and making the system more portable and flexible.

Spatial Frequency Multiplexing

The Medical Systems Division of the General Electric Corporation is interested in this project and has indicated in writing its intentions to vigorously pursue the commercial applications. G.E. has committed Ph.D.-level engineers and plans to invest a minimum of $30,000 in personnel and radiographic equipment support for further engineering and clinical experiments. In December, three G.E. physicists visited the Advanced Imaging Techniques Laboratory at Stanford University to further explore and negotiate a cooperative plan and to reaffirm their interest in this technology. This plan will be reviewed by their upper level management early next year and approval is anticipated.

NEW BIOMEDICAL ENGINEERING PROBLEMS

STANDARDIZATION AND INTERFACING OF REHABILITATIVE AIDS

Objective

To utilize the NASA expertise in the area of complex systems engineering to develop a coherent, broad solution to the problem of electronic-mechanical incompatibilities in the interfacing of multiple rehabilitative aids.

Background

It has been estimated that approximately 4% of the total U.S. population is functionally disabled to some degree (see attached table for breakdown of this figure). Such disabilities usually lessen an individual's potential for independent living and often relegate the disabled to the condition of decreased social interaction. Resultant isolation from community and friends greatly enhances the suffering of these individuals.

A substantial portion of this group would benefit considerably from a multifacted rehabilitative aid system, modular and adaptable in design, so that the elements of the system could be selected to serve a wide range of functional impairments. The modular elements of this ideal system would provide as needed such functions as:

1. Vocalization
2. Mobility
3. Telephonic communication
4. Environmental control
5. Self-instruction

TABLE 1

Number of Disabled People by Selected Types of Impairment and Age

(In Thousands)

	1	2	3	4	5	6	7	8
	Total	Under 17	17-44	Under 45	45-64	65 & Older	65-74	75 & Older
U.S. Population 1971	202,360	66,544	74,703	141,247	41,764	19,349	12,044	7,305
Blind and Visually Handicapped (all degrees of disability)	9,596	623	2,385	3,008	2,630	3,958	-	-
Blind and Visually Handicapped (causing limitation in activity)	495	-	-	54	99	342	-	-
Hearing Impairments (all degrees of disability)	14,491	863	3,167	4,030	4,765	5,695	2,783	2,912
Hearing Impairments (causing limitation in activity)	573	93	155	248	147	176	76	100
Speech Difficulty (all degrees of disability)	1,934	995	505	1,500	268	165	-	-
Speech Difficulty (causing limitation in activity)	188	57	29	86	54	46	-	-
Paralysis (all degrees of disability)	1,392	158	342	500	446	446	-	-
Paralysis (causing limitation in activity)	861	100	198	298	285	277	-	-
Absence of Major Extremity	274	-	-	70	127	77	-	-
Impairment of Back or Spine (all degrees of disabililty)	8,018	210	3,662	2,872	2,847	1,298	824	474
Impairment of Back and Spine (causing limitation in activity)	1,,976	55	857	912	776	288	189	99
Impairment of Upper Extremity and Shoulder, except paralysis or absence (all degrees of disability)	2,440	120	886	1,006	855	578	-	-
Impairment of Upper Extremity and Shoulder, except paralysis or absence (causing limitation in activity)	485	26	220	246	186	52	-	-
Impairment of Lower Extremity and Hip, except paralysis or absence (all degrees of disability)	7,387	1,281	2,544	3,825	2,017	1,544	853	691
Impairment of Lower Extremity and Hip except paralysis or absence (causing limitation in activity)	1,727	141	481	622	560	543	237	306

Note 1. Column 1 yields two totals: 45,532,000 disabled (all degrees of disability) and 6,579,000 disabled causing limitation in activity. This latter figure, approximately 3% of the total population, can be used as an estimate of those needing rehabilitation engineering services.

2. All data in this table were synthesized from the National Center for Health Statistics series on disability Series 10, Number 99, Tables 1, 2, 4, 5, 7, 9, 10, 11, and 13.

3. The total listed in column 1 may not equal the sum of items in columns 4, 5 and 6 due to rounding effects.

Unfortunately, the situation currently exists that, while there is a diverse selection of electronic and mechanical aids on the market, the interconnection of these aids to form a useful system often requires extensive re-engineering. Such modification results in a system that is both costly and can often be used only by similarly disabled people.

NASA Technology

With the space program as impetus, NASA has evolved very effective systems engineering methods to optimize the building of complex aerospace structures. This expertise is directly applicable to the development of a program of recommended design standards and electronic-mechanical interfaces for rehabilitative aids.

Approach

The Stanford BATeam (SBATeam) will assist the University of Wisconsin BATeam (UWBATeam) in the formulation of a recommended format of standards governing rehabilitative aid interconnection compatibility. The recommendation of the Children's Hospital at Standord and the Santa Clara Valley Medical Center will be evaluated by the SBATeam and included in the formulation of general standards.

Plan

The SBATeam will attend conferences and workshops which address the problem of interfacing and system development. The Team will also monitor several of the rehabilitative aid projects currently underway in the San Francisco Bay Area.

EMBOLECTOMY CATHETER

Objective

To apply NASA engineering and materials expertise to the development of a catheter for removal of circulatory obstructions nonsurgically.

Background

Radiologists can localize blood flow obstructions (blood clots or atherosclerotic plaques) in arteries and veins by injecting radiopaque contrast material through a flexible plastic tube (catheter). X-rays taken during this procedure reveal both the location and severity of the vascular obstruction. Current therapy involves anticoagulation and/or surgery (embolectomy or endarterectomy) for removal of the obstruction. The surgery required can be either major or minor depending upon the anatomical location of the obstruction.

I.F. Hawkins, M.D. (Chief of Angiography, Univ. of Florida Medical School) contacted our biomedical team in April, 1977 for assistance with this problem. After a medical literature search and discussion with leading investigators in this field, a problem statement soliciting potential solutions was sent to all NASA Field Centers. Suggestions and engineering drawings were received from the Marshall Space Flight Center and the Lewis Research Center. The proposed solutions were evaluated by our team and by Dr. Hawkins. Of the five designs proposed, the spiral catheter with oscillating linear motion and jet spray suggested by

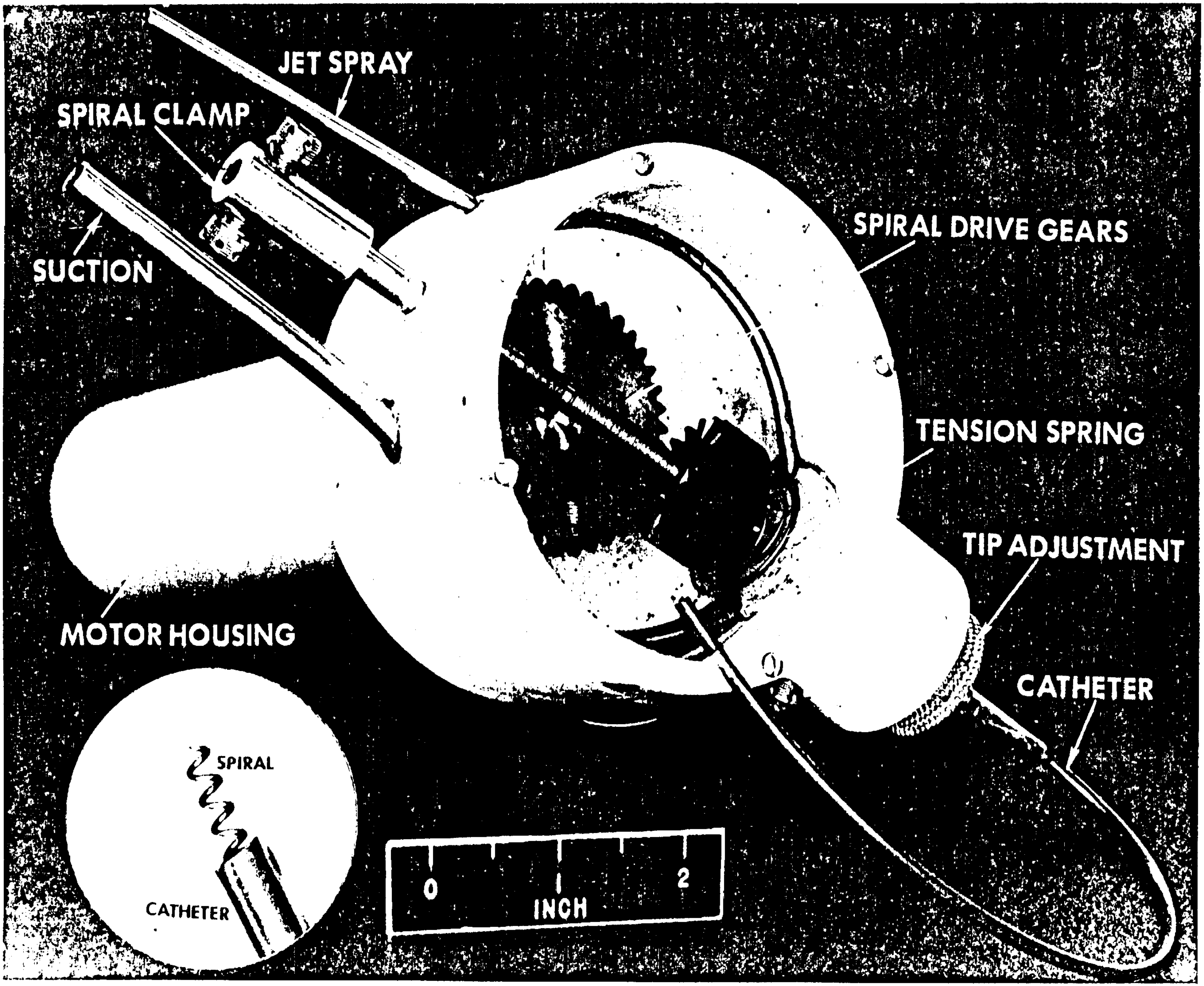


FIGURE 1 - TRANSLUMINAL ANGIOPLASTY DEVICE

Ray Helms at the Marshall Space Flight Center, was judged to have the highest probability of success. A prototype has been constructed and is shown in Figure 1. The catheter helix possesses an oscillating capability and the proximal end of the catheter incorporates a jet spray chamber to remove debris from the helix. An auger-type cutting tip attached to the distal end of the helix will be recessed just inside the catheter tip for removal of clots and plaques. A vernier will be used to protract the tip very slowly if a plaque is encountered. The helix will have a central lumen through which a guide wire could be passed to thread the catheter through tortuous areas of the vessel involved. A piggy-back tube could be attached for gas endarterectomy to loosen the plaque for removal via the Archimedes' screw-action of the helix.

Plans

A formal proposal has been approved by NASA Headquarters to further refine the prototype and to conduct preliminary tests in laboratory animals. However, Dr. Hawkins has recently decided to proceed with patent application on his own and does not wish to share the patent rights with NASA. He has declined any further formal NASA support or funding. Consequently, no further assistance will be provided by the BATeam or the Marshall Space Flight Center.

Stanford University School of Medicine
Biomedical Applications Team
Problem Statement

URETERAL STONE FRAGMENTATION CATHETER

Investigator -- Roger B. Goodfriend, M.D. FACS, Clinical Instructor of Surgery, Dept. of Urology; BA Team Contacts: Schmidt/ Zimmerman

I. Background:

The incidence of hospitalizations due to urinary calculi or stones has been estimated at 200,000 per year (H.L. Smith, Symposium on Stones. Amer. J. Med. 45: 649-653, 1968). Approximately 30 percent of patients with stones lodged in the ureter (the muscular tube which joins the kidney and the bladder) will be passed spontaneously. If the stone is small and is in the lower one-third of the ureter, an attempt may be made to remove it nonsurgically, using a Dormia stonebasket. This procedure is successful in approximately 50% of cases (Mahan, F. B. Critical Review of Stone Manipulation: A Five-Year Study. J. Urology 110:387-388, 1973). Basket manipulation of the stone frequently fails due to the stone being lodged in the upper ureter, the stone is too large (greater than one centimeter), or it has become impacted. In these cases the only way the stone can be removed is through a major surgical procedure called an open ureterolithotomy. This operation frequently requires an 8 to 12-day hospitalization followed by 6 to 8 weeks of convalescence.

The problem originator, assisted at sporadic intervals by three medical device manufacturers, has been developing a method for fragmenting ureteral calculi by means of an ultrasonically-driven wire probe which is placed in direct contact with the stone. Early prototypes consisted of a fine wire probe passed through a ureteral catheter until it made contact with the stone. Contact was verified radiographically. The ureteral catheter was then attached to a miniature pump through which an irrigating solution was delivered at a preset rate of flow. The wire probe was connected to an ultrasonic transducer which vibrated at 20 KHZ. The wire probe was advanced to protrude 2.0 mm. beyond the tip of the ureteral catheter. A contact force of 20 to 80 gm. was used. The probe was energized for three 3-second intervals. The multiple bursts of vibrational energy resulted in fragmentation of the stone and the smaller fragments can then be passed spontaneously.

This ultrasonically driven wire probe catheter developed by Dr. Goodfriend has been successfully used in fragmenting ureteral stones in several patients. The major difficulty has been in keeping the wire probe in constant contact with the stone. This has been accomplished by using X-ray and fluoroscopy. However, a better solution would be to directly visualize the stone through a fiberoptic system, thus eliminating X-radiation and increasing the certainty of direct coupling between the ultrasonic wire and the stone.

Two additional prototype sub-assemblies have been built and have been used clinically. One approach uses a joystick-steerable catheter, but lacks the fiberoptics. The second prototype is a fiberoptic ureteroscope, incorporating two small diameter bundles for illuminating and one 0.5 mm. diameter coherent bundle for visualization. It uses a lens which allows recognition of the stone from a distance of 0.5 to 10 mm.

II. Specific Needs:

A. Durable, Thin-walled Flexible Catheter Material

High frequency oscillations of the wire probe cause heating at the nodal points along the length of the catheter. Consequently, the presently used catheter material is short-lived and a better material is being sought. The catheter should have the following characteristics (see diagram):

a. It will need to incorporate four wires symmetrically spaced around the perimeter to provide for steerable control of the tip.

b. The maximum outside diameter would be 2.3 mm (#7 French)

c. An approximately 0.7 mm lumen for the coherent fiberoptic bundle (for viewing).

d. A 1.2 mm. lumen to allow for lateral vibrations of the 0.5 - 0.8 mm. diameter wire probe.

e. A small diameter lumen for the fiberoptic light source, illuminating bundle.

f. A small diameter lumen for irrigation.

g. The total length of the catheter will be 65 cm.

B. Presently an 0.8 mm. diameter wire probe is being used.

Stainless steel, titanium, and elgiloy have been tried. Elgiloy has been the most durable, however, it tends to fracture approximately 1.0 cm. beyond its coupling point to the ultrasonic driver where it is secured with a single set screw. Assistance is needed in reducing or eliminating this breakage problem. Possible solutions might include: choice of a more durable material, heat treating, or coating the elgiloy, a change in the thickness of the wire probe where it couples to the ultrasonic driver, or a change in the jig used to fix the end of the wire to the driver.

The following companies have worked on various components of this system, however, none at this point is able to integrate these components into a composite instrument. Problems (A) and (B) above are considered to be significant obstacles to the commercialization of this instrument and assistance from NASA Field Center engineers in selecting better material or materials configurations is essential to the transfer of this technology.

MEDITECH CORPORATION--Markets a steerable catheter.

AMERICAN OPTICAL--Maker of fiberoptic catheters has fabricated a fiberoptic ureteroscope.

BLACKSTONE ULTRASOUND--Manufactures the ultrasonic driver used in the system.

III. Specific Resources Available for Implementing Solutions:

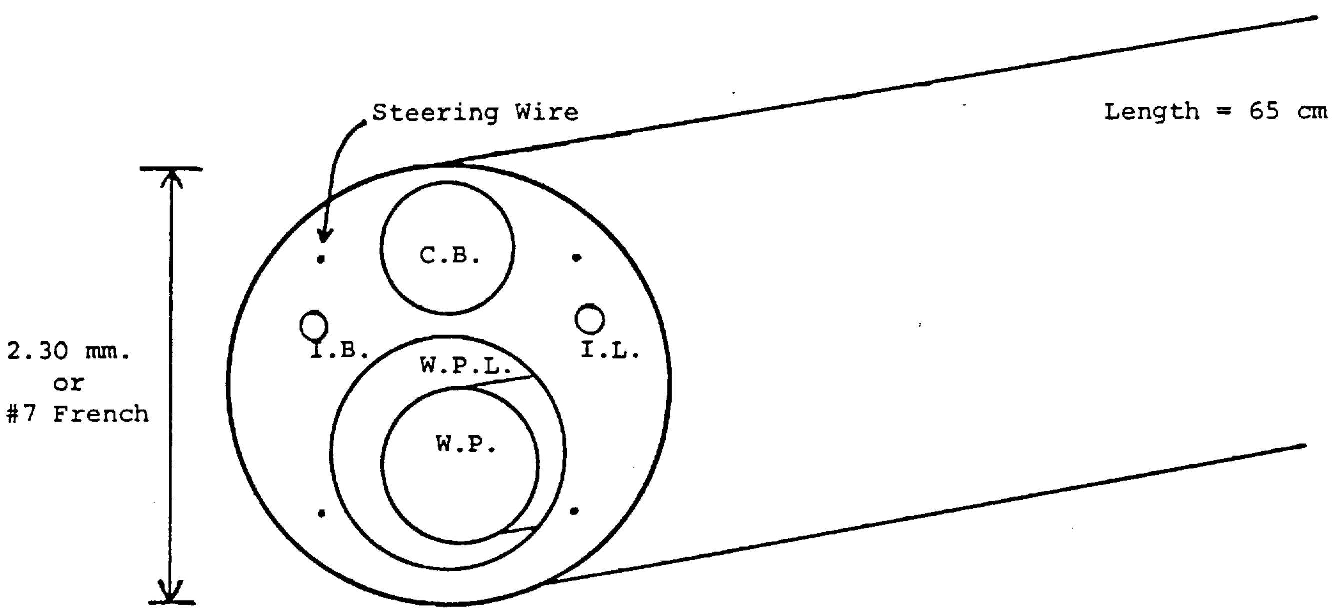
Dr. Goodfriend has animal laboratory facilities available to him for testing proposed solutions. He also has access to patients for demonstrating the clinical feasibility of this approach. Technical support in the form of suggestions for material and modifications of the system in the two problem areas (A) and (B) described above are needed. If NASA solutions appear promising, a proposal will be submitted to NASA T.U. Office to share in the funding of prototype fabrication and initial evaluation with industry.

IV. Suggested References:

1. Goodfriend, R.: Disintegration of Ureteral Calculi by Ultrasound, Urology, I (3):260-3, Mar. 73.
2. Mahan, F. B.: Critical Review of Stone Manipulation: A Five-Year Study Period, J. Urology 110:387-388,1973
3. Raney, A. M.: Electrohydrolic Lithotripsy: Experimental Study in Case Reports With Stone Disintegrator, J. Urology 113:345, 1975

4. Fair, H. D.: <u>In Vitro Destruction of Urinary Calculi by Laser-Induced Stress Waves</u>. Medical Instrumentation, vol. XII, no. 2; March-April, 1978.

Ureteral Stone Fragmentation Catheter



W. P.	=	Wire Probe	0.5 - 0.8 mm.
W.P.L.	=	Wire Probe Lumen	1.20 mm.
I.B.	=	Illuminating Bundle	diameter not critical
C.B.	=	Coherent Bundle	0.70 mm.
I.L.	=	Irrigation Lumen	diameter not critical

ADDENDUM TO URETERAL STONE PROBLEM STATEMENT

Information obtained by Paul Purser, BATeam consultant, per conversation with John Antonovich, Blackstone Ultrasound, on 18 September 1978:

Wire Probe

Vibrational characteristics:

The wire probe is secured to the ultrasonic horn via a set screw. The horn transmits longitudinal vibrations to the wire probe which, upon reaching the distal tip, become lateral and longitudinal vibrations. At a frequency of 20 kHz the longitudinal vibrations are 0.001 inch peak to peak. Fracture occurs after about 5 minutes, usually at a point 1/4-inch from the clamped end of the wire. At 20 kHz longitudinal vibrational nodes occur at 5-inch intervals and the wave propagation is 10^5 inches per second. It is desirable that the free distal end be an antinode since it is the lateral vibrations which cause the stone to fragment.

Dimension:

The wire probe currently used by Dr. Goodfriend is 65 cm. long, 0.022 inches (0.5 mm.) in diameter, and is made of Elgiloy, a cobalt-based alloy, which was developed for the wire springs used in Elgin watches. Ideally, the wire probe would have an even smaller diameter (e.g. 0.015 inches), which would permit the lumen to be smaller and allow the catheter wall to be thicker with more space for the fiber optics, irrigating lumen and steering wires.

Wire probe materials:

In addition to Elgiloy which is currently being used, the following meterials have been tried:

1. Titanium (Ti_6Al_4V) had the best acoustical characteristics but was too brittle.
2. Stainless steel (#316) was not as durable as Elgiloy.
3. Piano wire - Corrosion problem and was not as durable as Elgiloy.

Catheter Materials:

In order to accomodate the lumina for the wire probe and fiber optics, the catheter walls must be very thin and yet still withstand the heat generated by the vibrating wire. A catheter manufacturer is in the process of supplying some polyvinylchloride catheters; however, these have yet to be evaluated. Previously, Teflon has been tried; however, it was found to be too inflexible to negotiate the tight turns encountered at the ureter-bladder junction.

Status:

Dr. Goodfriend is in the process of tabulating data on the various catheter and wire probe materials used, their time to failure, and failure modes. This problem statement has been sent to all of the NASA field centers and a number of design and materials solutions have been received. In particular, Nitinol, a nickel and titanium alloy, has been suggested as wire probe material by the Chief of the Materials Control and Applications Branch at the Goddard Space Research Center. The Team has requested an IITRI market survey and will be preparing a proposal to NASA to implement its suggested solutions.

Stanford University School of Medicine
BIOMEDICAL APPLICATIONS TEAM
Problem Statement

I.D. # ______ Date: December, 1978

Multi-element Force Transducer for Mapping Sole Pressures
Problem Title

Michael J. Schaffer
Investigator

Bioelectronics Department
George Washington Univ. Medical Center
Institution/Department

Luke Brennan
BATeam Contact

Clinical Engineering
Field of Interest

I Background:

The diagnosis of podalic abnormalities would be significantly facilitated if the clinician could obtain data on plantar surface pressure distribution both while the patient is at stance and during ambulation. Low-resolution force plates have been fitted within shoes and special walkways. Unfortunately, these only provide an average resultant pressure of the entire foot and not a mapping of the local pressure valves. Enhanced resolution optical techniques have also been employed but these methods suffer from time-consuming instrumentation setup and film development.

II What is Needed (Specifically):

An inexpensive, multi-element force transducer which can be fabricated into an insole configuration. The elements should provide signals corresponding to local pressure valves which are to be sent to a data acquisition system. The evaluation of stance and gait abnormalities would be possible.

III Constraints and Specifications (Technical, Financial, and Temporal):

Thickness less than 1/4", minimal effect from humidity and temperature, and capability of each element to provide an indication preferably from 0-2000 psi, the latter being the greatest force expected during running or jogging.

701 Welch Road, Suite 3301, Palo Alto, CA 94304 - Phone: 415-497-5353

IV Specific Resources Available for Implementing Solutions Which May Be Offered:

Facilities	Staff	
___	___	Committed and Adequate
___	3	Available - To Be Scheduled
___	___	Must Be Acquired

Funding	
___	Existing
___	Pending
X	In-House
___	Request in Preparation
___	None

Comments:

Adequate staffing and funds are available.

V Past Solutions and Reason for New Solution:

Several instrumented shoes have been developed but none have been used successfully as a clinical tool because of poor accuracy and complicated operational procedure. A summary of some applied transducer methodology follows:

1. Variable Capacitance - Compressible dielectrics formed into insoles have been used. The variable capacitance property is incorporated into a circuit (oscillator). Stray capacitance is a problem as is the large transducer element size.
2. Pressure Variable Resistance - Elastomeric conductive material have been used in on/off switches. Difficulty in achieving uniform conductive properties throughout the material poses a problem.
3. Magnetostrictive Displacement - Too bulky for present application.
4. Strain Gauges and Piezoelectric Transducers - These methods show the most promise for incorporation into an insole unit.

VII Problem Status:

The currently proposed technique, using flexible printed circuits and coils etched on the surface, may be impractical due to the 10 mil. maximum width of the etching. With this limitation a 50 turn coil would require a diameter of 2".

The BATeam is currently reviewing field center response to this problem statement. Solutions will be solicited until March 1, 1979.

APPENDICES

APPENDIX A - COLLABORATING INSTITUTIONS

The following is an alphabetical list of non-NASA institutions, by project, that have been cooperating with the Stanford BATeam on various problem-solving activities during 1978:

Bone Mechanical Impedance

Departments of Orthopedics and Cardiology, Stanford University Medical School

Cardiovascular Magnetic Measurements

Physics and Cardiology Departments - Stanford University
Physics Department - Vanderbilt University, Nashville, TN

EMG Biotelemetry

Children's Hospital at Stanford - Palo Alto, CA
Ontario Crippled Children's Hospital - Ontario, CANADA

ICU Synthesized Speech Alarm System

Veterans Administration Hospital - Martinez, CA

Intracranial Pressure Monitoring

Departments of Anesthesia and Neurosurgery - Stanford University Medical School

Liquid Circulating Garments

Good Samaritan Hospital of Santa Clara Valley - San Jose, CA
Harbor General Hospital - Torrance, CA
National Cancer Institute - Bethesda, MD
University of Arizona - Tucson, AZ
University of North Carolina - Chapel Hill, NC

Nanophor

Clinical Laboratories, Stanford University Medical School

Pediatric Roentgen Densitometry

Columbia-Presbyterian Medical Center - New York City,NY
New York Medical College - Valhalla, NY
Peter Bent Brigham Hospital - Boston, MA

Purkinje Image Eyetracker

Eye Research Institute of the Retina Foundation - Boston, MA
National Eye Institute - Bethesda, MD
Santa Clara Valley Medical Center - San Jose, CA

Spatial Frequency Multiplexing

Departments of Engineering and Radiology - Stanford University

Transluminal Embolectomy-Angioplasty Catheter

Radiology Dept., Univ. of Florida Medical Center - Gainesville, FL

Ureteral Stone Disintegration

Department of Urology - Santa Clara Valley Medical Center, San Jose, CA

Versatile Portable Speech Prosthesis

Children's Hospital at Stanford - Palo Alto, CA

Wristcom

National Center for the Deaf-Blind - Long Island, CA
Smith-Kettlewell Institute - San Francisco, CA

APPENDIX B - MEDICAL DEVICE MANUFACTURERS

Below is a list of medical instrumentation manufacturers involved in the commercialization of technology derived from aerospace research and development as a result of Stanford BATeam projects:

1. Acurex/Aerotherm Corp.
   485 Clyde Ave.
   Mountain View, CA 94040
2. American Hospital Supply Corp.
   1015 Grand View Ave.
   Glendale, CA 91201
3. Blackstone Ultrasonics, Inc.
   Jamestown, NY
4. Federal Screw Works
   Vocal Interface Div.
   500 Stevenson Hwy
   Troy, NY
5. General Electric Co.
   Medical Systems Div.
   Milwaukee, WI
6. In Vivo Metric Systems
   P.O. Box 217
   Redwood Valley, CA 95470
7. Konigsberg Instruments, Inc.
   2000 East Foothill Blvd.
   Pasadena, CA 91107
8. L&M Electronics
   2401 Geneva Ave.
   Daly City, CA
9. Oxbridge, Inc.
   545 Weddell Dr.
   Sunnyvale, CA 94086
10. Pacesetter Systems, Inc.
    12740 San Fernando Road
    Sylmar, CA 91342
11. Plastics Technology
    Menlo Park, CA 94025
12. Radiologic Sciences, Inc.
    A Subsidiary of Pfizer, In.c
    2975 Scott Blvd.
    Santa Clara, CA 95050
13. RSY Associates
    P.O. Box 2756
    Evergreen, CO 80439

APPENDIX C - PROFESSIONAL PUBLICATIONS AND PRESENTATIONS

1. Quantitative Stability Measurement on Implantable Pressure Transducers - S.D. Corbin et al, AAMI 13th Annual Meeting.

2. Telemetry of Intracranial Pressure - T.B. Fryer et al, 4th International Symposium on Biotelemetry.

3. Workshop on Monitoring the Acutely Brain-Injured Patient - Bowman Gray Medical School, Winston-Salem, NC

   a. "Analysis and Meaningful Display of Patient Data" - Chairman, Gene Schmidt.

   b. "Intracranial Pressure Transducer - Monitoring Display" - Allen K. Ream.

4. Abstracts submitted for presentation and publication at the 4th International Symposium on Intracranial Pressure

   a. "A Capacitance Pressure Transducer to Measure Epidural Pressure" - S.D. Corbin et al.

   b. "Epidural ICP Biotelemetry - Bench Tests and Acute Animal Studies - E.V. Schmidt et al

   c. "Intracranial Pressure Monitoring: Chronic Animal Implantation and Preliminary Experience With an Implantable Telemetered System" - G.D. Silverberg et al.

5. Abstract submitted for presentation and publication at AAMI 14th Annual Meeting: "Intracranial Pressure Telemetry - Long-Term Bench Tests and Animal Studies" - E.V. Schmidt et al.

6. The Team is also in the process of preparing the proceedings of the international conference on NON-INVASIVE CARDIOVASCULAR MEASUREMENTS for publication by the Society of Photo-Optical Instrumentation Engineers (SPIE) in the spring, 1979.